Complete Summary

GUIDELINE TITLE

The management of diabetes mellitus in the primary care setting.

BIBLIOGRAPHIC SOURCE(S)

Management of diabetes mellitus in the primary care setting. Washington (DC): Department of Veterans Affairs (U.S.); 1999 Dec. 147 p. [185 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Diabetes mellitus

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Endocrinology
Internal Medicine

INTENDED USERS

Advanced Practice Nurses
Dietitians
Health Care Providers

Nurses
Pharmacists
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To promote evidence-based management of individuals with diabetes
- To identify the critical decision points in patient management such as glycemic control, evaluation of the eyes and feet, and early recognition and treatment of co-morbid conditions including hypertension, hyperlipidemia, and renal disease
- To allow flexibility so that local option and policies for implementation such as those regarding referral to or consultation with diabetes teams, ophthalmology, optometry, podiatry, nephrology, and endocrinology (lipids) can be accommodated
- To improve local management of patients with diabetes and thereby improve patient outcomes

TARGET POPULATION

Veterans with diabetes mellitus

INTERVENTIONS AND PRACTICES CONSIDERED

Core Assessment

1. Biochemical tests for diagnosis, including fasting blood sugar and random/casual blood sugar
2. Evaluation of symptoms and risk factors
3. Assessment of the risk of maternal fetal complications and screening of pregnant women for autoimmune thyroid disease, hypertension and renal disease
4. Identification of comorbid conditions and/or complications requiring special attention
5. Referral of pediatric patients
6. Patient stabilization (medically, psychologically, and socially)
7. Annual medical evaluation including: patient/family history, physical examination, laboratory tests, nutritional assessment, educational assessment)
8. Determination of diabetes type (Type 1 or 2, age, body mass index [BMI], urinary ketones)

Glycemic Control

1. Assessment of glycemic control (HbA1c), and the determination of optimal target HbA1c using risk stratification criteria
2. Adjustment of HbA1c target and target range according to individual risk, benefit and preference
3. Identification of high risk patients and patients requiring insulin therapy
4. Insulin replacement therapy (Type 1)

5. Pharmacological therapy (Type 2)
    - Sulfonylureas
    - Biguanides (metformin)
    - Insulin
    - Alpha-glucosidase inhibitor (miglitol, acarbose)
    - Thiazolidinediones (rosiglitazone, pioglitazone)
    - Repaglinide
6. Follow-up and patient monitoring
7. Patient education and practices to improve patient adherence
8. Referral to specialist, if necessary

Hypertension Management

1. Diagnosis of hypertension (blood pressure)
2. Identification of secondary causes of hypertension using laboratory tests
3. Identify manifestations of end organ damage/clinical cardiovascular disease
4. Diet and life style modification
5. Antihypertensive therapy:
    - Thiazides
    - Thiazides related (indapamide and metolazone)
    - Loop diuretics
    - Beta-blockers
    - Calcium channel blockers: Non-dihydropyridines (verapamil, diltiazem, mibefradil)
      Note: Dihydropyridines (nifedipine, amlodipine, nisoldipine, felodipine, isradipine, and nicardipine) are considered but not recommended
    - ACE inhibitors
    - Alpha-blockers
    - Angiotensin II Antagonists (losartan, valsartan, irbesartan)
    - Centrally acting beta-agonists (clonidine, guanabenz, methyldopa)
    - Other centrally acting agents (reserpine)
    - Direct vasodilating agents (minoxidil and hydralazine)
6. Follow-up and reevaluation
7. Referral to specialist, if necessary

Eye Care

1. Assessment of ocular risk factors and referral of high risk patients expediently for a dilated eye examination
2. Follow-up eye examination intervals
3. Patient education, including: the need for periodic eye examination, compliance, and the significance of new visual symptoms

Foot Care

1. Visual inspection and peripheral sensation testing at routine primary care visits, and annual foot risk assessment to identify patients at high risk for the development of foot ulcers and lower extremity amputations
2. Assessment of limb threatening conditions (e.g., systematic infection, acute ischemia or rest pain, foot ulceration, puncture wound, ingrown toenail, hemorrhagic callus with or without cellulites)

3. Wound assessment and the identification of any minor wound or lesion that can be treated by primary care physician
4. Referral to foot care specialist, when necessary
5. Patient and family foot education

Lipid Control

1. Diet and lifestyle modifications
2. Fasting lipid profile (total cholesterol, triglycerides, low-density lipoprotein, and high-density lipoprotein)
3. Assessment of glycemic control
4. Screening for excess alcohol (e.g., Michigan Alcohol Screening Test, Alcohol Use Disorders Identification Test) and cardiovascular disease
5. The American Heart Association (AHA) step II diet
6. Drug therapy (gemfibrozil, niacin)
7. Referral to lipid consultant, if necessary
8. Reassessment of lipid values at 3 and/or 6 months following initiation of therapy
9. Testing for thyroid stimulating hormone (TSH) level; thyroid treatment, if needed
10. Testing for nephrosis; referral to nephrologist, if necessary

Renal Disease Assessment/Treatment

1. Screening for renal disease (microalbuminuria; macroalbuminuria, microhematuria, renal insufficiency, nephropathy)
    - Routine urinalysis
    - Serum creatinine
    - Spot urine for albumin and creatinine
    - 24-hour urine for creatinine and protein
    - Random urine for protein/creatinine or albumin/creatinine ratio
2. Referral or consultation, if necessary
3. Evaluate for retinopathy and refer, if necessary
4. Treatment of transient causes of proteinuria
5. Re-evaluation for non-diabetic causes of elevated creatinine
6. Counseling patient on reduced protein diet
7. Identification of hypertensive patients who may benefit from hypertension control management
8. Drug therapy (ACE inhibitors) and periodic reevaluation (3 to 6 months)

Self-Management and Education

1. Education on basic concepts, core competency (survival skills), self-management, nutrition and/or other patient needs
2. Referral for comprehensive diet consultation, risk-focused intervention or to appropriate specialist
3. Assessment of patient's knowledge and self-management skills

MAJOR OUTCOMES CONSIDERED

- Blood glucose level
- Blood pressure

- Vision change
- Rates of foot wounds
- Lipid levels
- Identification of renal disease
- Level of patient knowledge of disease

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed a Medline literature search, dated March 1997 through March 1999, covering areas of diabetes, hypertension, lipid management, renal disease, foot and eye care, and diabetes education.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Grades of Evidence: Primary (Secondary)

A. Randomized (Other clinical studies)
B. Well designed clinical studies (Clinical studies related to topic but not in a population with diabetes)
C. Panel consensus (Clinical studies unrelated to topic)

Each of the references listed in the document have undergone a thorough review and rating based on the scientific rigor of the article, clinical relevance of the material presented and the ability to generalize using this data.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not applicable

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The original 1997 Veterans Health Administration (VHA) guidelines represented a "seed document" that was updated from January-June, 1999. As with the original workgroup, the charge of the VHA/Department of Defense (DoD) group was to provide evidence-based action recommendations whenever possible. Major clinical randomized controlled trials and observational studies published from March 1997 through March 1999 in the relevant areas were identified by the literature search and reviewed by the expert panel. Each reference cited was critically appraised for scientific merit, clinical relevance, and applicability to the populations served by the Federal health care system. Recommendations were based on the expert panels' opinion and clinical experience only when scientific evidence was unavailable from the current literature.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of Recommendation:

Level Ia: Usually indicated, always acceptable, and considered useful and effective.

Level IIa: Acceptable, of uncertain efficacy, and may be controversial. Weight of evidence in favor of usefulness/efficacy.

Level IIb: Acceptable, of uncertain efficacy, and may be controversial. May be helpful, not likely to be harmful.

Level III: Not acceptable, of uncertain efficacy and may be harmful. Does not appear in guidelines.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Comparison with Guidelines from Other Groups
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Version 1.0 of the VHA Guidelines was reviewed at a joint meeting of the National Diabetes Education Program (NDEP) Steering Committee and the Diabetes Mellitus Federal Interagency Coordinating Committee (DMICC) on October 21, 1997.

The original 1997 VHA guidelines represented a "seed document" that was updated and adapted by the joint VHA/DoD Diabetes Guideline Development Group over a six-month period from January-June, 1999.

This version was compared with the most recent guidelines published by other professional organizations, notably those of the American Diabetes Association, National Kidney Foundation (NKF), Joint National Council VI on Hypertension (JNC-VI), and National Cholesterol Education Program (NCEP). A summary comparing recommendations from VHA/DoD Diabetes Clinical Guidelines with other currently published guidelines is included in Table 2 in the original guideline document.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The recommendations for the management of diabetes in the primary care setting are organized into 8 major algorithms. Each algorithm, the objectives and annotations that accompany it, and the evidence supporting the recommendations are presented below. The strength of recommendation grading (I-III) and level of evidence grading (A-C) are defined at the end of the "Major Recommendations".

Note: A list of all abbreviations is provided at the end of the "Major Recommendations" field.

Core Algorithm

Module D - Core

This core module provides an overview of the important components of diabetes care that should be considered at each visit, and performed at appropriate intervals. Its objective is to assist the provider with the organization and prioritization of a care plan for persons with diabetes mellitus (DM).

A. Patient with Diabetes Mellitus

Diabetes mellitus is a state of absolute or relative insulin deficiency resulting in hyperglycemia. This algorithm applies to adults only (age $\geq$18), both type 1 and type 2 (formerly referred to as insulin-dependent and non-insulin dependent diabetes mellitus) but not to gestational diabetes mellitus (GDM).

Biochemical Criteria for Diagnosis

The criterion for the diagnosis of DM is either two fasting blood sugar readings with results $\geq$126 mg/dL or two random blood sugars with values $\geq$200 mg/dL, if symptoms of DM are present.

Oral glucose tolerance testing is no longer recommended in clinical practice. Hemoglobin A_1c (HbA_1c) measurement is not recommended as a screening

test. An individual with a casual plasma glucose level ≥200 mg/dL but without symptoms should have his or her fasting blood glucose measured.

Individuals with impaired glucose homeostasis have an increased risk of developing DM and should receive counseling regarding weight control, exercise, and future screening.

Diagnosis of Diabetes Mellitus

Status	Fasting Plasma Glucose (FPG) Preferred Level (a), (b)	Casual Plasma Glucose(c)
Diabetes mellitus	FPG >126 mg/dL (7.0 mmol/L)	Casual plasma glucose ≥200 mg/dL (11.1 mmol/L) plus symptoms
Impaired glucose homeostasis	Impaired fasting glucose (IFG) FPG ≥110; <126 mg/dL	
Normal	FPG <110 mg/dL	

(a) Fasting is defined as no caloric intake for at least 8 hours.
(b) FPG is the preferred test for diagnosis, but either of the two listed is acceptable. In the absence of unequivocal hyperglycemia with acute metabolic decompensation, one of these two tests should be used on a different day to confirm the diagnosis.
(c) Casual means any time of day without regard to time since last meal; classic symptoms include polyuria, polydipsia, and unexplained weight loss.

Patients with one or more of the following risk factors have a higher risk to be diagnosed with diabetes:

- Age ≥45 years
- Family history (parents or siblings with DM)
- High-density lipoprotein cholesterol (HDL-C) level ≥35 mg/dL (0.90 mmol/L) and triglyceride (TG) level ≥250 mg/dL (2.82 mmol/L)
- History of gestational diabetes mellitus (GDM); or women delivering babies weighing >9 pounds
- Hypertension (blood pressure ≥140/90 mmHg)
- Obesity (≥20 percent above ideal body weight, or body mass index (BMI) ≥27 kg/m2)
- History of impaired fasting glucose (IFG) or impaired glucose tolerance (IGT)
- Race/ethnicity: African American, Hispanic American, Native American, Asian American, Pacific Islander.

B. Refer to Pediatric Diabetes Management

Objective

To provide appropriate management for diabetic children

Annotation

Approximately three-fourths of all newly diagnosed cases of type 1 DM occur in children (below the age of 18). Children's health care needs are different from those of adults in several ways. Providing health care to children not only must involve meeting their physical needs but must address their changing developmental stages. It is important to remember that young children have a limited ability to communicate their needs and to indicate if they are in pain and therefore should not be expected to understand specific clinical interactions.

Primary care providers should refer children with diabetes for consultative care to a team with expertise in providing care to children. Members of this team must have knowledge of and experience in meeting the medical, psychosocial, and developmental needs of children. The pediatric diabetic team should comprise at a minimum, a pediatrician, a certified diabetes educator, a registered nurse, a registered dietitian, and a social worker, all with expertise and specialized training in the comprehensive care of the child with diabetes.

C. Is Patient a Female of Reproductive Potential?

Objective

To assess the risk of maternal fetal complications should unintended pregnancy occur and to implement prevention strategies

Annotation

Primary care providers should strongly recommend to all patients with pre-existing diabetes that they plan for and prepare for each pregnancy. Primary care providers should also counsel all diabetic female patients of reproductive potential on the need for optimal glycemic control.

Because of the high risk nature of the diabetic pregnancy and the need for intensive multidisciplinary monitoring and patient support, referral of diabetic patients to an expert high risk perinatal team at the earliest possible opportunity must be considered as the standard of care. Ideally, such referral should be made during the period of planned conception.

Evidence

Strength of Recommendation: I-IIb; Level of Evidence: B (Becerra et al., 1990; Lucas et al., 1989; Miller et al., 1981; Fuhrmann et al., 1983; Cousins, 1987).

D. Identify Comorbid Conditions

Objective

To evaluate DM management in the context of the patient's total health status

Annotation

DM may not be the patient's only disease, nor is it necessarily the condition that needs to be prioritized for immediate treatment. Persons with DM are at risk of multiple comorbid conditions including:

- Coronary artery disease (CAD)
- Peripheral vascular disease (PVD)
- Hypertension (HTN)
- Hyperlipidemia

The following are examples of conditions that affect the management of DM:

- Chronic obstructive pulmonary disease (COPD)
- Substance use disorder (SUD)
- Depression

Among the more frequently encountered precipitating factors resulting in secondary diabetes are:

- Pancreatic disease (e.g., due to alcoholism, pancreatic insufficiency secondary to chronic pancreatitis, malignancy, hemochromatosis)
- Drug induced disease (especially thiazide diuretics, steroids, phenytoin)

E. Is the Patient Medically, Psychologically, and Socially Stable?

Objective

To stabilize the patient before initiating long-term disease management

Annotation

- Urgent or semiurgent medical conditions, including hypo- or hyperglycemia, must be treated before long-term disease management principles are applied
- The urgency of medical treatment, including the necessity for hospitalization, will depend upon the presence of ketoacidosis, dehydration, hyperosmolarity, infections, etc.
- Psychiatric illness and marked socioeconomic hardship (homelessness, absence of support system, unemployment, absence of reliable transportation, etc.) pose significant barriers to diabetic management. If such circumstances are identified, involvement of mental health, social services, and case management professionals may enhance patient compliance with treatment and follow-up
- Stable condition represents the judgment of the provider

F. Identify/Update Related DM Problems from the Medical Record, History, Physical Examination, Laboratory Tests, Nutritional and Educational Assessment

Objective

To obtain and document a complete medical evaluation for the patient with DM annually

Annotation

In addition to a general medical examination, a complete evaluation of patients with DM will include:

- Information regarding the onset and duration of DM
- The history of hospitalization for diabetic events
- A review of glycemic control
- Measurement of serum lipids
- Identification of foot complications
- Identification of eye complications
- Screening for hypertension
- Screening for renal disease
- Identification of macrovascular disease
- Identification of neurovascular disease
- Assessment of psychosocial status (including family support)
- Appraisal of self-management skills

On a follow-up visit, the evaluation should focus on updating of new information and/or changes to the patient record. The components of evaluation are summarized in the table below.

Evaluation of the Diabetic Patient

Evaluation Component	History-Patient/Family	Physical Examination	Labo
Glycemia	• Home glucose monitoring records • Hyperglycemia • Ketoacidosis • Hypoglycemia • Lifestyle • Nutrition • Current and past medications Also consider secondary etiologies: • Cushing's disease • Acromegaly • Hemochromatosis • Medications	• Weight • Height • Body mass index (BMI) is calculated by dividing the patient's weight in kg by the patient's height, in meters squared.	• • g
Foot	Symptoms of neuropathy: pain, paresthesia Symptoms of peripheral	Visual inspection including: • Nails	N/A

	vascular disease Symptoms of systemic or local infection Previous episodes of foot complications: • Foot deformity • Skin breakdown • Ulcers • Amputations	• Web spaces • Ulcers • Calluses • Deformities Palpation of pulses and determination of sensation-consider using a 5.07 monofilament	
Eye	• Changes in vision • Laser treatment • Glaucoma • Dilated retinal exam by eye care provider within last year	Visual acuity, if changes in vision are reported	N/A
Kidney	• Known history of diabetic disease • Family history of hypertension and renal disease	Edema	• u • fc al a cr le in
Hypertension	• Previous diagnosis of hypertension • Current and previous medications	Blood pressure	N/A
Coronary and peripheral arterial disease/hyperlipidemia	Atherosclerotic disease: • Myocardial infarction (MI)/angina • Stroke • Transient ischemic attack (TIA) • Claudication • Surgical history of revascularization Atherosclerotic risks other than diabetes:	Cardiac examination: • Heart • Peripheral circulation including pulses and bruits • Cutaneous or tendinous xanthomata	• • li n w y

	• Smoking history • Family history • Previous diagnosis of hyperlipidemia; triglycerides Current and previous medications: • Aspirin • Estrogen therapy • Hypolipidemics		
Neurovascular	Sensory state of: • Hands and feet	• Interosseous muscle wasting • Deep tendon reflexes	N/A
Self-management education	Knowledge, understanding and self-described behaviors: • Use of medication • Goals of treatment • Diet and self management skills • What to do in case of complications	Observation: • Home glucose monitoring if indicated • Foot self-examination	N/A
Other	• Dental history and oral exam • Dental and gingival health • Infections • Insulin injection sites • Immunizations: flu, pneumovax	• Oral examination	N/A

Educational Assessment

Expert opinion led to development of the following questions that are believed to reflect the patient's general knowledge and ability to self-manage his or her diabetes adequately.

- Is there anything you do or have been advised to do because of your diabetes that you have difficulty with or are unable to do?

- Do you know what to do when your sugar is high/low (describe both hyperglycemia and hypoglycemia symptoms)? Who and when do you call?
- Do you remember your target goals: HbA_1c, low-density lipoprotein (LDL), weight, exercise, blood pressure?
- Which food affects your blood sugar the most: chicken breast, salad, or potato?

Inability of the patient to answer these questions indicates possible deficiency in knowledge and self-management skills. The clinician can refer to Module M (Self-Management/Education) for additional assessment and action plans.

Patients with DM who have more immediate medical or psychiatric problems should still have an educational need assessment done. This evaluation is to determine whether they have sufficient skills to manage their glycemic control during a period of concurrent illness, with a goal of avoiding symptomatic hypo- or hyperglycemia.

G. Determine and Document if Diabetes Mellitus is Type 1 or 2

Objective

To determine what treatment components are needed for a particular patient

Annotation

Patients with type 1 DM are insulinopenic (virtually absent insulin secretion), often due to autoimmune or toxic (e.g., alcohol) destruction of the pancreatic beta cells. Patients with type 2 DM have underlying insulin resistance and relative insulin deficiency.

In a primary care setting, determination of the patient's age at the diagnosis of DM, plus BMI, and level of urinary ketones, is usually sufficient to classify the patient.

Clinical Classification of DM

	Likely Type 1	Indeterminate	Likely Type 2
Age	<30 years	30 - 40 years	>40 years
BMI	<25 BMI	25 - 27	>27
Urinary ketones	Moderate to large	Low to moderate	None to low

H. Review Systems and Set Priorities for Patient's Care

Objective

Identify DM related complications requiring special attention

Annotation

Diabetes is the major cause for non-traumatic amputations, end-stage renal disease, and visual loss. In addition, the major cause of morbidity and mortality in diabetic patients is macrovascular disease. Effective strategies exist for preventing or treating micro- and macrovascular complications, thereby delaying or preventing end organ damage.

The provider and the patient must jointly negotiate the sequence and timing of the various assessments. Further, prioritization should be based on the risk of the individual patient for that complication.

This guideline recommend annual assessment of foot, lipid and renal function; annual exam eye (biannual for low risk patients); measurement of blood pressure at each office visit as well as reinforcement of life style, nutritional and exercise as appropriate. Glycemic control is recommended at each routine visit or any visit that relates to other concurrent problems.

If the assessment reveals any complication in any of these risk areas, further evaluation and management is indicated. The provider should then follow the appropriate module.

Algorithm - Glycemic Control

Module G - Glycemic Control

A. Patient with Diabetes Mellitus

Every patient with diabetes mellitus (DM), regardless of its duration, needs to negotiate with his or her provider an appropriate target glycemic goal and then plan a treatment strategy to achieve this goal.

Glycemic control should be reevaluated at every regular interim visit or in the context of visits that relate to other concurrent problems that could affect glycemic control.

B. Assess Glycemic Control

Objective

To determine the patient's current level of glycemic control

Annotation

Glycosylated hemoglobin measured or reported as hemoglobin HbA_1c, is the only laboratory test measure validated in controlled, randomized clinical trials as a predictor of risk for microvascular complications. Hence, periodic measurement of HbA_1c is recommended to assess glycemic control over time.

C. Determine recommended Glycemic Control Target Using Risk Stratification Criteria

Objective

To assess the risk of the patient for developing visual loss, renal insufficiency, and amputations

Annotation

Determination of an optimal target HbA_1c level is based upon the risk for developing microvascular complications. The individual risk is dependent on life expectancy, absence or presence of pre-existing microvascular complications, and genetic factors.

The likelihood of developing microvascular complications is largely dependent on how high the individual's glucose level has been and for how long. The duration of glycemic exposure, is like smoking duration for cancer risk; the severity of hyperglycemia is like the number of packs of cigarettes smoked daily. HbA_1c level is the best measure of the severity of hyperglycemia over time. The presence and stage of microvascular complications reflects prior duration and severity of hyperglycemic exposure, and individual susceptibility to development of complications.

The glycemic target range must be individualized for each patient based on the clinician's appraisal of the risk-benefit ratio for that individual. Additionally, following counseling, the patient's own preferences should be factored into the decision-making. The risks and benefits of a target value must be determined mutually by both the provider and the person with diabetes in the context of the proposed therapeutic regimen as well as patient preferences.

In general, patients with very mild or no microvascular complications of diabetes and those free of major concurrent illnesses adversely affecting quality of life and survival are most apt to benefit from intensive treatment intended to achieve near-normoglycemia. Conversely, patients with advanced microvascular complications and/or major comorbid illness may be less likely to show survival benefit, may continue to show progression of microvascular disease, and frequently may be at increased risk for severe hypoglycemic morbidity when normoglycemic control is attempted.

In the absence of a readily available mechanism to assist the provider in the estimation of life expectancy. The table below is intended to provide an overall perspective. To aid the clinician in counseling diabetic patients about individual glycemic control goals, the table provides a decision making matrix that considers microvascular complications and comorbid illness.

Determination of Target HbA_1c Level

Major Comorbidity (d) or Physiologic Age	Microvascular Complications		
	Absent or Mild (a)	Moderate (b)	Advanced (c)

Absent (>15 years of life expectancy)	7 percent (<1 percent above upper normal range)	<8 percent (<2 percent above upper normal range)	<9 percent (<3 percent above upper normal range)
Present (e) 5 to 15 years of life expectancy	<8 percent (<2 percent above upper normal range)	<8 percent (<2 percent above upper normal range)	<9 percent (<3 percent above upper normal range)
Marked (f) <5 years of life expectancy	<9 percent (<3 percent above upper normal range)	<9 percent (<3 percent above upper normal range)	<9 percent (<3 percent above upper normal range)

(a) Mild microvascular disease is defined by early background retinopathy, and/or microalbuminuria and/or mild neuropathy
(b) Moderate microvascular disease is defined by pre-proliferative (without severe hemorrhage, intra-retinal microvascular anomalies (IRMA), or venous bleeding) retinopathy or persistent, fixed proteinuria (macroalbuminuria) and/or demonstrable peripheral neuropathy (sensory loss)
(c) Advanced microvascular disease is defined by severe non-proliferative (with severe hemorrhage, IRMA, or venous bleeding) or proliferative retinopathy and/or renal insufficiency (serum creatinine level >2.0 mg/dl) and/or insensate extremities or autonomic neuropathy (gastroparesis, impaired sweating, orthostatic hypotension, etc.)
(d) Major comorbidity includes, but is not limited to, any or several of the following conditions: cardiovascular disease, chronic obstructive pulmonary disease, chronic liver disease, stroke, malignancy
(e) Moderate degree of major comorbid condition
(f) Severe degree or end-stage major comorbid condition

Evidence

Progression to non-proliferative retinopathy: Strength of Recommendation: I; Level of Evidence: A (Diabetes Control and Complications Trial [DCCT] Research Group, 1993; Ohkubo et al., 1995; Klein et al., 1995).

Progression to Proliferative Retinopathy: Strength of Recommendation: I; Level of Evidence: B (Klein et al., 1994).

Progression to microalbuminuria: Strength of Recommendation: I; Level of Evidence: A (DCCT Research Group, 1993; Ohkubo et al., 1995; Kawazu et al., 1994), B (Krolewski, 1996).

Progression to proteinuria: Strength of Recommendation: I; Level of Evidence: A (DCCT Research Group, 1993; Ohkubo et al., 1995).

Progression to blindness: Strength of Recommendation: I; Level of Evidence: A (DCCT Research Group, 1993; Ohkubo et al., 1995).

Progression to end-stage renal disease: Strength of Recommendation: I; Level of Evidence: C (DCCT Research Group, 1993; Ohkubo et al., 1995; Klein et al., 1995).

Progression to neuropathy: Strength of Recommendation: I; Level of Evidence: A (DCCT Research Group, 1993; DCCT, 1995).

Progression to amputations: Strength of Recommendation: I; Level of Evidence: B (Klein et al., 1994; Mayfield et al., 1996).

Myocardial infarction, stroke: Strength of Recommendation: IIb; Level of Evidence: A (DCCT Research Group, 1993; Ohkubo et al., 1995), B (Anderson et al., 1995; Singer et al., 1992; Klein et al., 1995).

Effect of DM on life expectancy: Strength of Recommendation: I; Level of Evidence: B (Panzram et al., 1987; Goodkin, 1975; Singer, 1992).

Duration of DM and incidence of end-stage microvascular complications: Strength of Recommendation: I; Level of Evidence: B (Klein et al., 1994, 1995; Palmberg et al., 1981; Humphrey et al., 1989).

Effect of ethnicity on glycemic target levels: Strength of Recommendation: IIa; Level of Evidence: B (Haffner et al., 1988; Haffner et al., 1989; Lee et al., 1992; Nelson et al., 1988; Rabb et al., 1990).

Pre-existing retinopathy or microalbuminuria as a risk factor for progression: Strength of Recommendation: I; Level of Evidence: A (DCCT Research Group, 1993, 1995; Ohkubo et al., 1995).

Progression to microvascular complication (primary laser therapy): Strength of Recommendation: I; Level of Evidence: A (UKPDS, 1998).

D. Adjust the Glycemic Target According to Patient's Factors

Objective

To ensure that the recommended target value for HbA_1c can be safely achieved by the patient, taking into consideration individual risk, benefit, and preference

Annotation

The risks of therapy are different for each patient, depending upon the individual's medical, social, and psychological status. Thus, the risks of a proposed therapy must be balanced against the potential benefits.

E. Set Target Range After Discussion with Patient

Objective

To establish the patient's readiness and willingness to achieve the target

Annotation

Target range of glycosylated hemoglobin based upon life expectancy, microvascular complications, and familial history, is a starting point for negotiation with the patient. It does not mean that a lower HbA_1c level will not be beneficial, nor does it mean that the provider and the patient should not negotiate a lower one. Rather, it implies that there is a decreased benefit of excellent glycemic control in the setting of limited survival expectation or pre-existing moderate-to-advanced microvascular complications of diabetes. These factors should be taken into account when evaluating the risks and benefits of pharmacological therapy as well as patient preferences. In addition, it should be recognized that reduction in risk from decreasing HbA_1c is a continuum, so a negotiated target level does not have to be exactly 7.0, 8.0, or 9.0 percent. The patient should make the final decision as to a specific target value of glycemic control after a full discussion of the risks and benefits of therapy with his or her provider.

Providers should consider that some patients may require more immediate, urgent, or aggressive management in primary care. Some cases may require referral to an endocrine/diabetes clinic, or to a case manager in order to meet glycemic control target goals.

F. Is Patient High Risk?

Objective

To identify high risk patients for whom subspecialty consultation would be appropriate to assist in the development of a treatment plan and/or to supervise ongoing care

Annotation

High risk DM patients include those who:

- Have type 1 DM (especially patients with history of hospitalizations for metabolic complications and/or patients who are receiving intensive insulin therapy)
- Have recurrent episodes of incapacitating hypo- and/or hyperglycemia
- Have poor recognition of hypoglycemia and who have history of severe hypoglycemic reactions (including coma, seizures, or frequent need for emergency resuscitation)
- Have new-onset insulin-requiring DM
- Have visual and/or renal impairment
- Have psychosocial problems (including alcohol or substance abuse) that complicate management
- Have HbA_1c >9.5 percent

The Diabetes Quality Improvement Project (DQIP), a federal/private sector coalition, reached the consensus that HbA_1c >9.5 percent represents high-risk glycemic control even in the absence of case mix adjustment. Consequently, providers should consider a patient with HbA_1c >9.5 percent for aggressive management on an expedited basis. Patients who are on high-dose multiple agents should also be consider for referral.

G. Does Patient Require Insulin?

Objective

To identify patients for whom insulin treatment is the only viable alternative

Annotation

All patients with type 1 DM by definition must receive insulin therapy. Additionally, patients with type 2 diabetes or diabetes of undetermined cause who exhibit significant or rapid weight loss and/or persistent non-fasting ketonuria have at least severe relative insulin deficiency and will require insulin therapy on an indefinite basis.

Weight loss and ketonuria are indications of a catabolic state for which insulin is preferred therapy in type 2 DM. Insulin is an anabolic hormone, and is often beneficial in such circumstances, especially if there is a concurrent illness.

H. Institute/Adjust Insulin, Consider Referral

Objective

To improve/achieve glycemic goals using insulin

Annotation

Because type 1 DM is caused by absolute insulin deficiency, insulin replacement therapy is the only viable treatment option. Insulin therapy for patients with type 1 DM must be individualized and customized according to multiple lifestyle factors. Institution and adjustment of insulin therapy is most efficiently accomplished by referral to a diabetic clinic with multidisciplinary resources including diabetologists, diabetic nurse, educator/managers, and registered dietitians. If expedient referral cannot be accomplished, the primary care provider should institute "survival" insulin therapy. This can be initiated at a calculated total daily dose (TDD) of 0.5 units/kg body weight/day. Two-thirds of the TDD administered 30 minutes prior to breakfast as two parts human NPH insulin and one part human regular insulin. The remaining thirds of the TDD can be split equally, as human regular insulin 30 minutes before supper and as human NPH insulin at bedtime.

See Appendix G3 of the original document, Insulin Therapy.

I. Assure Appropriate Intervention to Address Patient Adherence

Objective

To assure proper patient monitoring and contact with the health care team

Annotation

An important touchstone for successful management of type 2 diabetes is comprehensive patient education and internalization of self-management knowledge and performance skills (see Module M). Ongoing professional contact allows for feedback, answering questions, reinforcing positive skills and behaviors, and improving suboptimal skills and behaviors. Ideally, the diabetes nurse educator/manager and dietetic consultant will be involved as partners with the primary care provider. Together they should assess the patient's knowledge, performance skills, and barriers to full compliance. If psychosocial, personal, or financial barriers are identified, additional resources, such as mental health, medical social work, or financial counselors can be consulted as applicable.

J. Initiate/Adjust Therapy

Objective

To achieve glycemic target goals by the most cost effective and least invasive means

Annotation

Long-term outcomes (survival and occurrence of microvascular complications) of treatment of DM are related to the degree of glycemic control achieved, but not to the means used to achieve control (diet/exercise vs. oral hypoglycemic agent vs. insulin, or any known combination therapy). Based on this principle, therapy should be tailored to individual preferences, needs, and pragmatic considerations, such as cost and ease of compliance.

Each newly diagnosed patient with DM should attempt non-pharmacological treatment with diet and lifestyle modification prior to use of medications. There is considerable evidence from the UKPDS that type 2 DM is a progressive disease, which will necessitate the adjustment of medication dosage and additive pharmacological therapy over time. The table below summarizes a concept of sequential treatment commonly employed in clinical practice.

Recommended Option for Type 2 DM

Therapy	Drugs	Expected reduction in HbA1c Over a 2 to 3 month period of follow-up

Lifestyle modification, diet and exercise	None	
Lifestyle modification, diet and exercise Monotherapy with oral agent	Sulfonylurea or biguanide	1-2 percent
Lifestyle modification diet and exercise Combination (add a second oral agent)	Sulfonylurea + biguanide Sulfonylurea or biguanide + alpha-glucosidase inhibitor Sulfonylurea or biguanide + thiazolidinedione Biguanide + repaglinide	1-2 percent 0.5 to 1 percent 0.7 to 1.75 percent 0.1 to .3 percent
Insulin with oral agent	Biguanide + insulin Thiazolidinedione + insulin Sulfonylurea + insulin	
Insulin	Insulin alone	
Referral		

- Individual treatment goals must be established with the patient based on the extent of the disease, comorbid conditions, and patient preferences.
- Institution of diet and exercise is usually the appropriate initial management in patients with new onset type 2 diabetes, depending upon severity of symptoms, pyschosocial evaluation, and overall health status. Encourage diet and exercise and lifestyle modification.
- If treatment goals are not achieved with diet and exercise alone, a sulfonylurea or biguanide (i.e., metformin) should be used as first line drug therapy. For patients with significant obesity, initial monotherapy with a biguanide may be preferable.
- If the glycemic target level is not achieved with either agent alone, a biguanide (i.e., metformin) may be combined with a sulfonylurea.
- Alpha-glucosidase inhibitors may be used in conjunction with a sulfonylurea or sulfonylurea/biguanide combination in patients whose postprandial blood glucose is inadequately controlled but whose fasting glucose is in the desired range on sulfonylurea or sulfonylurea/biguanide regimens.
- Addition of bedtime insulin therapy to an existing combination oral agent regimen may be a treatment option when the glycemic control target is not achieved by an all-oral regimen.
- In patients treated with large doses of insulin, addition of a thiazolidinedione may reduce the insulin requirement and produce

improved glycemia, with reduction of HbA_1c by 1 to 2 percent. Thiazolidinediones are not recommended as first-line monotherapy.

- Intermediate-acting insulin in a single evening dose may be used in conjunction with oral monotherapy with either sulfonylurea or biguanide, or in addition to combine sulfonylurea/biguanide therapy. It may also be used as a single agent, when given in multiple daily doses, if the glycemic control target has not been reached with oral therapy. The use of insulin Lispro is not recommended for routine use in treatment of type 2 DM, as there is no evidence that it has any inherent superiority to less costly insulin preparations.
- Carefully selected individuals may benefit from three-drug oral hypoglycemic therapy. In general, such patients may benefit from referral to a diabetes care team.
- Patients who fail to attain target glycemic control goal despite ongoing care, education, and medication adjustment in the primary care setting may benefit from referral to a diabetes care team for comprehensive assessment and intensified management.

There is no evidence that blood glucose monitoring in stable type 2 DM patients is of clinical benefit. If self-monitoring is to be done, a twice-weekly regimen is usually sufficient. Special situations, such as acute intercurrent illness, frequent hypo- or hyperglycemia, or changes in medication regimen, may justify more frequent monitoring on a temporary basis.

See Appendix G4 of the original document, Pharmacological Therapy.

K. Determine If There Are Side Effects or Contraindications to Current Treatment

Objective

To modify therapy due to side effects of drug therapy

Annotation

Side effects of pharmacological therapy can include drug-drug, hypoglycemia, and specific adverse drug effects. Patients may experience side effects from medications if adjustments are not made when patients undergo medical or surgical procedures, have a change in their condition, or develop an intercurrent illness.

Patients with recurrent or severe hypoglycemia should be evaluated for precipitating factors that may be easily correctable (e.g., missed meals, incorrect administration of insulin (dosage or timing), exercise, etc.). In many cases, a simple adjustment can be made in nutrition, exercise, medication and/or patient self-monitoring. In patients with near-normal glycemic control (notably patients with type 1 DM on intensive insulin treatment or patients with autonomic neuropathy), it may be necessary to relax the degree of glycemic control, at least temporarily. Complex adjustments may best be accomplished through co-management with a diabetes team.

Certain drug effects, e.g., gastrointestinal symptoms, may improve over time or with modification of the dosage regimen and thus may not necessitate discontinuance of medication. On the other hand, some drugs may have adverse effects that require vigilant monitoring, such as frequent measurement of serum liver function tests in patients treated with troglitazone. Finally, patients may develop contraindications to continued use of a previously successful maintenance medication. Examples would include newly recognized renal insufficiency or severe congestive heart failure in a patient treated with metformin.

See Appendix G4 of the original document, Pharmacological Therapy.

L. Are There Problems with Patient Adherence?

Objective

To identify barriers to full adherence to the prescribed treatment regimen

Annotation

It is appropriate to briefly review adherence to the prescribed nutritional and exercise regimens as well as to review the dosages and timing of administration of medication. If the patient does not achieve his or her target range, the practitioner should look for barriers to patient adherence to regimen. Barriers may include miscommunication, lack of education, lack of understanding, financial or social barriers, psychological barriers and cultural beliefs (e.g., learned helplessness). In addition, the patient may have treatment preferences that are not being addressed.

The patient may be considered for case management or referral to a behavioral or a financial counselor, as appropriate.

See Module M, Patient Self-management and Needs Assessment.

M. Should Glycemic Control Target Be Adjusted?

Objective

To determine whether the recommended glycemic control goal remains appropriate for the patient

Annotation

Treatment goals should be periodically reassessed based upon patient specific factors, including changes in patient health status, adverse drug reactions, adherence to therapy, and preferences.

Relative indications for raising the target glycemic goal include inability or unwillingness to adhere to a more intensive regimen, or an unacceptable risk of hypoglycemia relative to anticipated benefits of near-normal glycemia.

If the target range remains appropriate but has not been reached, the provider and patient should identify the reasons why the target has not been achieved and take appropriate action.

Reasons to consider lowering the target glycemic control goal include removal of barriers to improved control (e.g., substance abuse, intercurrent illnesses, adherence issues) and resolution of relative contraindications. See also annotation D above.

N. Follow-Up

Objective

To maintain glycemic control and ensure proper patient monitoring by the health care team

Annotation

The patient should be scheduled for appropriate follow-up to evaluate response, tolerability to therapy, goal re-assessment and management of acute and chronic problems. The frequency of primary care provider visits for the diabetic patient who is meeting treatment goals and who has no unstable chronic complications should be individualized. When there is a sudden change in health status or when changes are made to the treatment regimen, follow-up within one month or sooner may be appropriate.

Algorithm - Hypertension Management

Module H - Hypertension Management

A. Patient with Diabetes Mellitus and High Blood Pressure (SBP ≥140 DBP ≥ 85)

Normal blood pressure (BP) for adults is ≤130/85 mmHg and high normal BP is 130-139/85-89 mmHg. There is evidence to suggest that decreasing BP to ≤130/85 mmHg is beneficial in diabetes mellitus (DM), and even lower BP goals (125/75 mmHg) have been suggested in patients with proteinuria (>1g/24 hours).

Classification of Blood Pressure in Adults (a)

Category	Systolic	Diastolic
Normal	≤130 mmHg and	≤85 mmHg
High-normal	130-139 mmHg or	85-89 mmHg
Hypertension (b)		
Stage 1	140-159 mmHg or	90-99 mmHg
Stage 2	160-179 mmHg or	100-109 mmHg
Stage 3	≥180 mmHg or	≥110 mmHg

(a) Adapted from The Sixth Report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure 1997
(b) Based on the average of two or more readings taken at each of two or more visits.

Evidence

Classification of blood pressure: Strength of Recommendation: I, Level of Evidence: C (Sixth Report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure, 1997); Strength of Recommendation: I, Level of Evidence: A (Hansson et al., 1998; UKPDS, 1998).

B. Is a Secondary Cause Suspected?

Objective

To identify patients with an underlying disease process responsible for their HTN

Annotation

Although fewer than five percent of all patients have secondary HTN, clinicians should constantly be alert for secondary causes, as many of these are reversible. Secondary HTN should be suspected for patients with:

- Abrupt onset of HTN
- Drug resistant HTN
- Sudden loss of BP control after a history of good pharmacological control
- Other factors that contribute to HTN include substance abuse, diet, caffeine, salt, steroids, and psychosocial stressors

See Table H2 of the original document for selected causes and clinical features of secondary hypertension

Refer to Annotation I below for causes of inadequate response to therapy.

C. Continue Evaluation and Treatment as Indicated. Consider Referral to Appropriate Specialist to Manage Secondary Cause(s)

Objective

To detect underlying disease(s) responsible for secondary HTN using additional laboratory tests

Annotation

An early discussion or consultation with an appropriate specialist is encouraged when a patient is suspected of having secondary hypertension.

This may lead to the most accurate and cost-effective workup if an underlying cause of HTN is suspected.

The following tests may be helpful in determining the need for referral.

Recommended Testing for Patients Suspected of Having Secondary Hypertension

Disease	Recommended Test/Referral
Cushing's syndrome	24-hour urine for free cortisol
Hyperaldosteronism	Serum potassium
Hyperparathyroidism	Serum calcium and parathyroid hormone (PTH) level
Hyperthyroidism/Hypothyroidism	Thyroid Stimulating Hormone (TSH)
Pheochromocytoma	24-hour urine for metanephrines or urinary catecholamines Consider referral to specialist
Renal parenchymal disease	Urinalysis, urine sediment, serum creatinine, 24-hour urine for protein and creatinine clearance or spot urine for Alb/Cr ratio Consider referral to nephrology
Renovascular disease	There are a variety of screening tests for renovascular HTN, depending on equipment and expertise in institutions There is no single best test for renovascular HTN Consult experts in your institution IVPs are relatively contraindicated in diabetes
Sleep apnea	Referral for sleep reference

D. Hypertension with End Organ Damage or Strong Indication for Therapy?

Objective

To identify manifestations of target organ disease/clinical cardiovascular disease

Annotation

Existing target organ damage should be specially investigated in the following organ systems:

- Cardiac
- Cerebrovascular
- Peripheral vascular
- Renal (see Module R)
- Ophthalmic (see Module E).

See Table H4 in the original document for a list of manifestations of target organ disease

E. Consider Aggressive Life Style Modification With/Without Drug Therapy

Objective

To induce life style modifications that will lower BP

Annotation

There is evidence that BP can improve with:

- Smoking cessation
- Increased physical activity (if sedentary)
- Limitation of alcohol intake
- Weight reduction (if obese)
- Moderation of dietary sodium
- Stress management.

See Module M, Self-management and Patient Education.

F. Measure Blood Pressure at Each Office Visit

Objective

To properly monitor BP at each office visit

Annotation

Blood pressure should be measured at each office visit. When initiating or changing therapy, blood pressure measurements obtained in alternative settings (other clinics, pharmacies, home, etc.) may be reviewed and considered.

When monitoring blood pressure in patients with diabetes, it is important to check for orthostatic hypotension. Patients with autonomic neuropathy are at increased risk for developing orthostatic hypotension. In all patients who have diabetes, blood pressure should be measured periodically in the supine, sitting, and standing positions.

G. Is Blood Pressure Control Adequate?

Objective

To assess the effectiveness and tolerability of BP-lowering treatment

Annotation

The goal of the intervention is to maintain BP at or below 140/90 mmHg. There is evidence suggesting that achieving a BP $\leq$130/85 mm Hg may offer increased benefits. Attaining a lower BP target (125/75 mmHg) is recommended for patients who have proteinuria (>1 g/24 hours) or renal insufficiency. The clinician should monitor for and avoid symptoms of orthostatic hypotension, congestive heart failure (CHF), angina, or significantly worsened renal function (Sixth Report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure [JNC-VI], 1997).

H. Initiate/Continue Drug Therapy

Objective

To lower BP using antihypertensive medication.

Annotation

Lifestyle modifications that can lower blood pressure are described in Annotation E. For continuous monitoring of blood pressure, see Annotation F. Many medications are available for the treatment of HTN.

Current recommendations for drug therapy are:

- Angiotensin converting enzyme (ACE) inhibitors (2), beta-blockers, alpha-receptor blockers, diuretics in low doses and angiotensin 2 receptor antagonists are preferred because of fewer adverse effects on glucose homeostasis, lipid profiles and renal function.
- Short-acting dihydropyridine calcium-channel blockers as monotherapy have been reported as associated with increased risk of cardiovascular complications, and therefore are not preferred first-line agents.
- Beta-blocker therapy should be considered if coronary artery disease is present.
- If proteinuria or renal disease is present, use ACE inhibitors as first-line treatment of HTN.
- If congestive heart failure is present, consider ACE inhibitors and diuretics.
- If systolic dysfunction is present, use ACE inhibitors preferentially.

Evidence

Strength of Recommendation: I; Level of Evidence: A (Estacio et al., 1998; Tatti et al., 1998; Cameau et al., 1997; Hunninghake et al., 1994; UKPDS 38, 39, 1998), C (JNC-VI, 1997).

When choosing an antihypertensive medication, the potential adverse effects of the medication need to be considered. Some of these cautions are reviewed (see the original document) for each class of medication.

I. Titrate Initial Drug, Add or Substitute Another Agent. Reassess Adherence, Weight, Alcohol, Acute Life Stresses, and Medical Problems. Reinforce Lifestyle Modification. Consider Referral to Specialist

Objective

To identify causes of inadequate response to therapy

Annotation

If blood pressure control is inadequate, the dose of the initial drug can be titrated, or an agent from another class of drugs can be added. If a drug is not well tolerated, substitution of an agent from another class may be considered.

Poor adherence to antihypertensive therapy remains a major therapeutic challenge. Aside from simple inadequacy of the chosen agent, the clinician should consider alternate explanations for inadequate response to drug therapy. These include medical or psychiatric conditions that undermine blood pressure control.

Poor patient response to the initial drug management strategy should always lead the primary care provider to explore several important factors that may explain failure to achieve target blood pressure.

See Table H5 of the original document for a list of causes of inadequate response to therapy

Algorithm - Eye Care

Module E - Eye Care

A. Has Patient's Vision Changed Recently?

Objective

To identify patients with diabetes mellitus (DM) in need of urgent referral to an eye care provider

Annotation

Any acute change in vision or change in ocular function should prompt an urgent referral to an eye care provider.

B. Reassess Need for Eye Examination within 1 Year

Objective

To establish the timing of the initial ocular evaluation for patients with early-onset DM

Annotation

For patients with onset of diabetes prior to the age of 30, the risk for retinopathy becomes significant after 3 to 5 years of disease.

Evidence

Strength of Recommendation: I; Level of Evidence: B (Klein et al., 1984).

C. Is Any Ocular Risk Factor Present?

Objective

To identify patients at risk for advanced retinopathy or rapid progression of pre-existing diabetic eye disease

Annotation

High risk patients present with one or more of the following:

- DM for 15 years or more
- Gross proteinuria ($\geq$200 microgram/min)
- Dialysis dependent
- Status post renal transplantation
- Type 2 DM and cardiovascular autonomic neuropathy
- Lower extremity amputation related to DM
- History of laser therapy for retinopathy
- Diabetic and pregnant

D. Refer for Eye Examination Within 1 Month

Objective

To ensure that high risk patients are referred expediently

Annotation

Patients considered at high risk for ocular complications must be seen expediently and receive a comprehensive dilated eye examination by an eye care specialist (ophthalmologist or optometrist) knowledgeable and experienced in the detection of diabetic eye disease.

Evidence

Strength of Recommendation: I, Level of Evidence: B (Nathan et al., 1991).

E. Is Patient Newly Diagnosed Type 2 DM or on Insulin Therapy?

Objective

To identify high risk patients who have not had a dilated eye examination within the previous 12 months

Annotation

The inability of symptoms alone to accurately predict the presence or severity of retinopathy necessitates timely referral to an eye care provider for patients who have not had a dilated eye examination within the previous 12 months and who have no established examination schedule.

Evidence

Strength of Recommendation: I, Level of Evidence: B (Klein et al., 1989).

F. Follow-Up Examination Yearly or According to Eye Care Provider-Recommended Schedule

Objective

To establish a follow-up interval for patients requiring insulin or whose disease is not well controlled

Annotation

Patients who have no evidence of retinopathy on dilated fundus examination are unlikely to develop vision-threatening disease within a 12-month period.

Evidence

Strength of Recommendation: I, Level of Evidence: B (Javitt, Conner, & Sommer, 1989; Javitt et al., 1994; Dasbach, 1991; Morisaki et al., 1994; Chen et al., 1995).

G. Patient has maintained HbA_1c >8.0

Objective

To identify DM patients who do not require insulin and whose disease is not controlled

Annotation

Older onset patients not requiring insulin and who are able to maintain an HbA_1c level below 8, are at lower risk than other diabetics to develop advanced retinopathy.

Algorithm - Foot Care

Module F - Foot Care

A. Perform and Document Visual Inspection of Feet

Objective

To examine the feet for any grossly abnormal findings

Annotation

Inspect the feet for:

- Breaks in the skin
- Erythema
- Trauma
- Pallor on elevation
- Dependent rubor
- Changes in the size or shape of the foot
- Nail deformities
- Extensive callus
- Tinea pedis
- Pitting edema

B. Perform Foot Risk Assessment

Objective

To identify those patients who are at risk for lower extremity (LE) ulcers and amputations

Annotation

The foot risk assessment must be performed and documented at least once a year. The yearly foot risk assessment includes:

- Evaluation of the skin for breakdown
- Assessment of protective sensation
- Evaluation for LE arterial disease
- Evaluation for foot deformity
- Prior history of ulcers or amputations

In addition, evaluate the patient's footwear.

C. Are Any Limb Threatening Conditions Present?

Objective

To be alert for patients that may have a limb-threatening condition that may require immediate attention, referral and or hospitalization

Annotation

- Systemic or ascending (worsening) Infection?

  Limb threatening conditions could include signs and symptoms of systemic infection including gas gangrene, ascending cellulitis and lymphangitis or gangrene.

  Although infection is not always clinically apparent, common signs and symptoms include periulcer area warmth, erythema, purulent drainage, odor and involvement of bone. Pain may or may not be present. There may or may not be lymphangitis and lymphadenopathy, fever and white blood cell count may or may not be present. Sudden loss of glycemic control often heralds serious infections.

  Evidence

  Assessment of peripheral vascular disease in diabetes: Strength of Recommendation: IIa, Level of Evidence: C (Orchard & Strandness, 1993).

- Acute Ischemia or Rest Pain?

  Absence of palpable pedal pulses:

  Examine the patient to determine presence of dorsalis pedis and posterior tibial pulses. No palpable pulses and signs of acute ischemia, e.g., resting pain associated with extreme pallor or palpably cold extremities, warrant urgent referral to a vascular surgeon.

  Acute ischemia or rest pin - evidence of arterial insufficiency:

  Lower limb pain at rest, dusky/blue or purple/black color, gangrene, or cold extremity. The pain in the toes or forefoot may be relieved by dependency of the limb in the early phases. Assessment is needed for prompt vascular/surgical intervention. Acute ischemic or avascular foot will "present with" pain, pallor, pulseless, paresthesia and/or paralysis.

  Claudication:

  Severe claudication is determined as pain in the thigh or calf that occurs when walking less than 1 block and is relieved by rest.

  Evidence

Strength of Recommendation: IIa, Level of Evidence: C (Orchard & Strandness, 1993).

- Foot Ulceration?

  Active foot ulcer: A cutaneous erosion with a loss of epithelium that extends to or through the dermis, can involve deeper tissue and is characterized by an inability to self-repair in a timely and orderly manner.

  Evidence

  Strength of Recommendation: I-IIa; Level of Evidence: C (Reiber et al., 1995; American Diabetes Association [ADA], 1990; Eckman et al., 1995; Brodsky et al., 1991; Caputo et al., 1994).

- Puncture Wound?

  Diabetic patients with puncture wounds can quickly develop severe limb threatening complications. A lesion through the epidermis, dermis and other tissues caused by a piercing or penetrating object.

- Ingrown Toenail?

  An ingrown toenail presents as a nail plate that has pierced the surrounding periungual tissue with associated erythema and drainage or an area of thick or discolored callus. The primary care provider should consider referral to a podiatrist for excision of infected ingrown nails, especially in the case of high risk patients.

  Evidence

  Strength of Recommendation: IIa, Level of Evidence: B (Giacalone, 1997).

- Hemorrhagic Callus With or Without Cellulitis?

  The provider must determine if the cellulitis maybe associated with callus tissue or necrotic tissue that may obscure an underlying ulceration or deeper infection.

  The callus tissue must be debrided to properly assess the extent of an underlying ulceration and possible deeper more serious infection. Necrotic tissue must also be debrided to help eradicate the infection and determine the full extent of the infection. These patients should be referred promptly to a foot care specialist for complete evaluation and treatment.

D. Refer To Appropriate Level Of Care For Evaluation And Treatment

Objective

To determine the appropriate intervention

Annotation

A foot care specialist is defined as a podiatrist, vascular surgeon, orthopedic surgeon, or other health care provider with demonstrated training, competence and licensure in foot care.

If the patient's symptoms limit his or her lifestyle, a vascular specialist can determine appropriateness of surgical intervention on a patient-specific basis.

Evidence

Justification of vascular procedures based on outcomes of vascular interventions. Strength of Recommendation: IIa, Level of Evidence: A (Wolf et al., 1993), B (Currie et al., 1995), C (Conte, 1995; Lavery et al., 1995).

E. Is Patient at High Risk for Foot Problem?

Objective

To identify patient at high risk for lower extremity foot ulcers and amputations

Annotation

The presence of any of the following characteristics equals high risk:

- Lack of sensation to Semmes-Weinstein 5.07 monofilament at one or more noncallused plantar sites.
- Evidence of lower extremity arterial disease:
    - Absence of both dorsalis pedis and tibialis posterior pulses
    - Dependent rubor or pallor on elevation
    - History of rest pain or claudication
    - Prior history of lower extremity bypass surgery.
- Foot deformities, specifically hammer toes, claw toe, Charcot's arthropathy
- History of foot ulcer or non-traumatic lower extremity amputation at any level.

Patient at high risk should be referred to a foot care specialist for a more intensive treatment plan of in-depth patient education concerning foot care practices, hygiene and footwear.

Evidence

Strength of Recommendation: I-IIb, Level of Evidence: B (Boyko et al., 1996; Mayfield et al., 1996; Rith-Najarian et al., 1992; Pecoraro et al., 1990), C (ADA, 1990; Bailey, Yu, & Rayfield, 1985; Birke et al., 1988; Holewski et al., 1988; Sims, 1988).

F. Is There a Minor Wound or Lesion?

Objective

To determine the extent of the injury

Annotation

Minor lesions or wounds that could possibly be treated by the PCP are blisters, erosions, and/or minor cuts that do not extend beyond subcutaneous tissue. Pulses are present, there are no signs of acute infection, and there is no severe lower limb pain and no sign of a worsening lesion. An ingrown toenail should be referred to a foot specialist for evaluation and excision. (See Annotation C5, Ingrown Toenail.)

G. Refer promptly to foot care specialist for complete evaluation and treatment.

Objective

To ensure more intensive follow up treatment plan

Annotation

A foot care specialist is defined as a podiatrist, vascular surgeon, orthopedic surgeon, and other health care provider with demonstrated training, competence and licensure in foot care.

Mechanical modalities may include footwear recommendations, and consideration of a footwear prescription will be based upon the individual structural and clinical findings. Depth shoes should be prescribed for a patient with foot deformities and peripheral neuropathy as they can accept pressure-reducing insoles and accommodate foot deformities. In-depth shoes usually have soft leather uppers paired with a crepe or Vibram outsole. Custom-molded shoes are reserved for patients with foot deformities that cannot be accommodated in a depth shoe.

Persons with diabetes should avoid shoes with hard soles, since they do little to reduce plantar foot pressures. Running shoes have been shown to reduce plantar pressures in individuals with diabetes; however, they may not accommodate foot deformities.

H. Perform and Document Patient Education for Preventive Foot Care and Footwear

Objective

To empower the patient to perform proper foot care practices

Annotation

Patient/Family education for preventive foot care and footwear includes:

- Daily foot inspection and preventive care
- Skin, nail and callus care
- What to report and whom to call regarding any foot injury or abnormality
- Footwear: Reduction of lower extremity clinical abnormalities in patients with NIDDM.

See the original document for specific components of patient and family foot education.

Evidence

Strength of Recommendation: I-IIa, Level of Evidence: A (Litzelman et al., 1993), B (Uccioli et al., 1995), C (ADA, 1999; Cavanagh et al., 1987; Perry et al., 1995; Perry et al., 1995; Young et al., 1992).

Patient self-foot care instruction: Strength of Recommendation: I, Level of Evidence: B (Barth, 1991), C (Feste, 1991; Fain, 1994; Ahroni et al., 1993; Weir et al., 1994).

I. Perform Visual Inspection And Peripheral Sensation at Each Routine Primary Care Visit

Objective

To ensure ongoing screening to identify those patients at risk for lower extremity ulcers and amputation

Annotation

Follow-up includes:

- Yearly foot risk assessment - Every individual with diabetes must have had a documented foot risk assessment within the past 12 months to determine their risk of lower extremity amputation
- Visual inspection and peripheral sensation testing at routine primary care visits - There is limited information, yet consensus exists in the diabetes professional community that visual inspection combined with peripheral sensation testing may reveal some occult lesions in diabetics. This practice also demonstrates to the patient the importance of foot assessment.

J. Perform Wound Assessment

Objective

To determine character and nature of wound

Annotation

- Review anatomic, physical, and lesion characteristics, including determination or circumference, depth, and involvement of deep structures.
- Assess for signs of infection, including necrosis, sinus tracts, exudate, odor, presence of fibrin, and healthy granulation tissue.
- Assess surrounding areas for signs of edema, cellulitis, or abscess.

K. Provide Local Wound Care, Offload Pressure and Weight as Indicated

Objective

To provide care of an uncomplicated minor lesion

Annotation

The following are simple guidelines for the care of uncomplicated minor lesions:

- Provide local wound care: Cleanse wound with saline, remove necrotic and callus tissue, apply appropriate dressing and other indicated treatments.
- Offload pressure and weight as indicated: Consider lesion site, and then provide pressure relief, e.g., special shoes and insoles, bed rest, etc. To avoid further trauma to lesion site by use of post-operative shoe, offloading or depressurization footwear based on lesions site.
- Follow up on a specified schedule: VA facility specific patients, but with active lesions need to be followed at least monthly.
- Review self-management and education module: Reinforce nutritional, exercise and self-management recommendations. Avoid initiation of calorie restriction diet for weight loss in patients with foot lesions.
- Provide patient and family education.
- Refer for foot care assistance as needed for patients unable to do local wound care. Educate a family member on local wound care or refer the patient to a home health service.

Evidence

Strength of Recommendation: IIa, Level of Evidence: C (ADA, 1990; Eckman et al., 1995; Brodsky, 1991; Caputo et al., 1994).

L. Has Wound Healed Within 4 Weeks?

Objective

To determine appropriateness of the treatment outcome

Annotation

Uncomplicated wounds should heal in a timely fashion. Assess for appropriate reduction in lesion size and depth and appearance of healthy granulating tissue, with no evidence of infection.

Evidence

Progress for Wound Healing: Strength of Recommendation: IIa, Level of Evidence: B (ADA, 1999), C (ADA, 1990).

M. Is There a Minor Foot Problem?

Objective

To identify minor conditions that could be attended to by the patient and/or family member

Annotation

Assess feet for presence onychomycosis, painful corn dry skin, athlete's foot, minor calluses, uncomplicated nail trimming and proper foot hygiene.

N. Treat as Appropriate

Objective

To determine the feasibility of treating the patient at home or in the office of the primary care provider

Annotation

Many minor foot problems can be treated by the patient and/or family members, or primary health care providers without referral to foot care specialists. If this approach is chosen, it is necessary that the patient and family members have received appropriate education regarding preventive foot care.

Evidence

Strength of Recommendation: I, Level of Evidence: B (Barth, 1991), C (Feste, 1991; Fain, 1994; Ahroni, 1993; Weir et al., 1994).

Algorithm - Lipid Control

Module L - Lipid Control

A. Patient with Diabetes Mellitus and Dyslipidemia

Objective

To concentrate efforts on those patients likely to benefit from management of lipids

Annotation

Efforts to adjust serum lipid levels should be focused on those who are likely to live more than 5 years.

Evidence

Absence of a relationship between serum cholesterol level and CHD/mortality above age 70 years. Strength of Recommendation: I, Level of Evidence: B (Krumholz et al., 1994).

Indication to assess lipid levels in older patients who appear younger than their actual age and are otherwise in good health: Strength of Recommendation: IIa, Level of Evidence: = C (National Cholesterol Education Program [NCEP-II], 1993).

B. Provide and Document Counseling

Objective

To promote lifestyle changes that will decrease CVD risk.

Annotation

There is reasonable evidence that some interventions lower the risk of CVD.

There is evidence that CVD risk is improved with:

- Smoking cessation
- A low-fat, low-cholesterol diet
- Exercise
- Limitation of alcohol intake to one or two drinks per day
- Weight loss if overweight
- Stress management

Evidence

Lifestyle changes reduce risk for CVD: Strength of Recommendation: I, Level of Evidence: C (NCEP-II, 1993).

C. Obtain Lipid Profile TC/TG/LDL/HDL Measured In Fasting State

Objective

To measure reliably the level of serum lipids when indicated

Annotation

Most treatment sites offer a lipid profile that includes reporting the LDL-C level. The lipid profile should be done at least twice before using the data to make a therapeutic decision. If the LDL-C measurements differ by more than 30 mg/dL, a third test should be obtained within one to eight weeks and the

average of the three values used. Lipids should not be measured in acutely ill patients or for 1 or 2 months after a hospital discharge, as acute illness can effect an accurate measurement.

With the results, one can determine whether serum lipids constitute a significant risk factor for CVD in a patient and set a baseline for future change if specific therapy is started.

Evidence

Strength of Recommendation: I, Level of Evidence: C (NCEP-II, 1993).

D. Is Triglyceride Level >400 mg/dL?

Objective

To determine whether the TG level is high enough to require specific attention

Annotation

A clearly elevated TG (>400 mg/dL) may predispose the diabetic patient to CVD as well as to pancreatitis, and may require drug therapy if not manageable by other means.

Evidence

Classification of TG levels: Strength of Recommendation: I, Level of Evidence: C (NCEP-II, 1993).

E. Optimize Glycemic Control

Objective

To assess the effect of glycemic control on the TG level

Annotation

Poor glycemic control can cause elevated triglycerides. Better glycemic control may result in lowering the TG level.

Evidence

Effect of intensive diabetes management on macrovascular events and risk factors: Strength of Recommendation: I, Level of Evidence: A (DCCT, 1995; Stone, 1997).

F. Screen for Alcohol Use

Objective

To determine whether alcohol intake is the cause of an elevated TG level.

Annotation

Alcohol intake can be the cause of a high TG level. If alcohol intake is excessive (more than two drinks per day in men and, more than one drink per day in women, where a drink is defined as 1 oz of hard liquor, 3.5 oz of wine, or 12 oz of beer), then appropriate counseling needs to be offered.

Evidence

Strength of Recommendation = I, Level of Evidence = C (Stone et al., 1997).

G. Is Cardiovascular Disease Present?

Objective

To determine what the target LDL-C level should be in a patient with diagnosed CVD and institute the most appropriate medical therapy

Annotation

The NCEP-II recommends a target LDL-C of 100 mg/dl or below for patients with known cardiovascular disease. No definitive LDL-C goal has been defined by prospective clinical trials. Several large, randomized, double-blinded, placebo-controlled studies support the idea that aggressive lowering of LDL-C in these patients significantly reduces major coronary events but the absolute level is still under debate.

H. Initiate AHA Step II Diet. Provide Education and Life Style Counseling.

Objective

To assess the effect of more intensive nutrition and life style counseling on elevated lipid levels

Annotation

In some patients, extra effort toward changing nutrition and life style factors may succeed in lowering the LDL-C even when usual efforts at lifestyle change have not.

Evidence

Strength of Recommendation: I, Level of Evidence: C (NCEP-II, 1993).

I. Consider Drug Therapy or Refer to Lipid Consultant

Objective

To identify factors determining pharmacological management and referral to a lipid consultant

Annotation

Diabetics with dyslipidemia without secondary cause (see annotations N and O) are candidates for pharmacological management or referral to a lipid specialist in order to achieve lipid goals. Most patients can be treated by the primary care provider. However, it remains the prerogative of the primary care provider to refer the patient if the provider is not comfortable with the pharmacological options. Once the decision has been made to use pharmacological therapy, the patient is essentially committed to a lifetime of drug therapy. The decision, therefore, must be carefully undertaken.

J. Initiate/Modify Drug Therapy to Decrease Triglycerides

Objective

To lower a clearly raised TG level

Annotation

With continued elevation of the serum TG level, pharmacological therapy to lower TG or referral to a lipid consultant is appropriate.

K. Evaluate for Potential Complications of Drugs. Reassess Lipid Values at Three and/or Six Months. Readjust Medication if Indicated

Objective

To provide adequate monitoring of drug effects and side effects

Annotation

Antilipidemic drugs can have side effects, principally on liver function. Furthermore, these drugs need to be assessed in relation to the LDL-C goal.

L. Reassess Lipids Within One Year

Objective

To follow-up lipid testing when LDL-C is within goal and the TG level is not clearly raised

Annotation

When the LDL-C level is 130 mg/dL or less and the TG level is not clearly raised, e.g., <400 mg/dL, lipid levels should be reassessed at least annually.

Evidence

Annual reassessment of lipid profiles for any patient with two or more CVD risk factors: Strength of Recommendation: I, Level of Evidence: C (NCEP-II, 1993).

M. Is LDL-C >130 mg/dL?

Objective

To determine the LDL-C level above which persons with DM type 2 are likely to be at increased risk for CVD

Annotation

This level (>130 mg/dL of LDL-C) represents the approximate level at which patients with DM type 2 may benefit from a lower LDL-C.

N. Is Thyroid Stimulating Hormone (TSH) High?

Objective

To detect and, if needed, treat hypothyroidism as a contributor to a raised LDL-C level

Annotation

Hypothyroidism is a known secondary cause for elevated LDL-C. If the thyroid-stimulating hormone (TSH) level is clearly high, the patient should be treated for hypothyroidism.

Evidence

Strength of Recommendation: I, Level of Evidence: C (Stone et al., 1997; NCEP-II, 1993).

O. Is Nephrosis Present?

Objective

To determine whether nephrosis is present as a potential cause of an elevated LDL-C

Annotation

Nephrosis is a secondary cause of dyslipidemia and an assessment is indicated when searching for secondary causes of abnormal lipid levels. Nephrosis is characterized by excessive urinary protein excretion, which may be detected by routine "dipstick" urine testing. If the test is positive on two occasions, a quantitative 24-hour measurement of urine protein needs to be done.

Evidence

Strength of Recommendation: I, Level of Evidence: C (Stone et al., 1997; NCEP-II, 1993).

Algorithm - Renal Care

Module R - Renal Disease

A. Patient with Diabetes Mellitus

Objective

To screen for renal disease in patients with diabetes mellitus (DM)

Annotation

Patients with type 1 DM should be screened for renal disease after puberty and at a minimum of every five years of duration. Patients with type 2 DM should be screened for renal disease at the time of DM diagnosis because the onset of type 2 DM occurs on average 10 years before clinical diagnosis is made (Harris, 1995).

B. Obtain Routine Urinalysis (for assessing proteinuria)

Objective

To screen for macroalbuminuria and microhematuria in patients

Annotation

If the protein level is 1+ or greater on routine urinalysis, the patient already has macroalbuminuria and using a more sensitive test to check for microalbuminuria is unnecessary. If the red blood cells (RBC) are > 4 to 5 per high field (HPF), evaluate appropriately.

On the typical dipstick for routine urinalysis (e.g., Combistix), protein readings are:

1+ = 30 mg/dL
2+ = 100 mg/dL
3+ = 300 mg/dL
4+ = 1,000 mg/dL

C. Obtain Serum Creatinine

Objective

To detect presence of significant renal insufficiency

Annotation

The serum creatinine distinguishes patients with severe from those with mild to moderate chronic renal insufficiency.

D. Is Serum Creatinine $\geq$2.0 mg/dL?

Objective

To identify individuals with moderate to severe renal insufficiency in need of immediate evaluation

Annotation

Serum creatinine $\geq$2.0 mg/dL indicates a substantial loss of remaining functional units in the kidney. These individuals may already be developing secondary complications and be in need of a nephrologist's assessment or co-management. Waiting to treat nephropathy until the serum creatinine level rises above normal range is not likely to prevent end-stage renal disease, but rather just delay the need for dialysis a few more months.

E. Consider Referral or Consult with Nephrologist/Dietitian

Objective

To decide whether referral is needed for either diagnostic or co-management reasons

Annotation

Referral to or consultation by telephone with a nephrologist may be helpful to the primary care physician to jointly manage:

- Electrolyte disorders (hyperkalemia, acidosis)
- Secondary hyperparathyroidism
- Anemia secondary to erythropoietin deficiency
- Fluid overload
- Preparation for dialysis access, including development of forearm muscle mass and preservation of vascular access site (no needle sticks)
- Immunizations, including Heptovax.

There also is a need to treat high blood pressure aggressively and to lower potassium and protein content of the diet to delay the need for dialysis Without intervention, progression to end-stage renal disease can occur rapidly. In addition, reversible causes of elevated creatinine need to be investigated, such as urinary tract obstruction or acute glomerulonephritis. The nephrologist can be consulted to assist in this workup. If a telephone consultation is used, it is advisable to document the conversation in the patient's medical record (Bennett, 1995).

F. Is Serum Creatinine >1.4 but <2.0 mg/dL?

Objective

To identify individuals with moderate renal insufficiency in need of further diagnostic workup

Annotation

Patients with a serum creatinine level between 1.4 and 2.0 mg/dL also have significant renal disease but are less likely to have electrolyte disturbances, anemia, or bone disease than those with a creatinine level of $\geq$2.0 mg/dL. If diabetic nephropathy is the cause of the elevated creatinine, the patient is likely to have all of the following:

- Macroalbuminuria ($\geq$300 mg/24 hours)
- Some evidence of diabetic retinopathy
- Normal size kidneys

With regard to the natural history of the disease, even if the patient was not previously hypertensive, his or her blood pressure is likely to begin increasing at this stage. If proteinuria is in the nephrotic range (>3g/24 hours), the patient may also develop peripheral edema or anasarca.

Evidence

Strength of Recommendation: IIa, Level of Evidence: C (ADA, 1997; Bennett et al., 1995).

G. Identify and Treat Transient Causes of Proteinuria

Objective

To identify and treat potential non-diabetic causes of proteinuria

Annotation

"Heavy exercise, urinary tract infection, acute febrile illnesses, and heart failure may transiently increase urinary albumin excretion and thus, screening should be postponed in these situations." This Panel does not recommend stopping an ACE (angiotensin-converting enzyme) inhibitor in screened patients already being treated with this medication. This Panel recommends instructing patients not to exercise the day before providing a specimen.

Factors that Transiently Interfere with Urinary Screening for Albuminuria

Increases in Albuminuria	Decreases in Albuminuria
Blood in urine Congestive heart failure	ACE inhibitors Malnutrition

Exercise Excessive protein intake Fever Uncontrolled diabetes Uncontrolled hypertension Urinary tract infection Vaginal fluid contamination of specimen NSAIDs	Nonsteroidal anti-inflammatory drugs (NSAIDs)

Evidence

Strength of Recommendation: I, Level of Evidence: C (ADA, 1996; Bennett et al., 1995).

H. Is Probable Life Expectancy ≥5 Years?

Objective

To determine if patients with proteinuria are likely to live long enough to develop renal disease

Annotation

Diabetic nephropathy develops 5 to 20 years after the diagnosis of DM. Patients who do not already have proteinuria are not likely to develop end-stage renal disease in less than 5 years.

Evidence

Strength of Recommendation: IIa, Level of Evidence: C (Bennett et al., 1995; Mogensen, 1987; Gall, 1991; Ordonez, 1989).

I. Measure Spot Urine for Albumin and Creatinine

Objective

To screen for early nephropathy

Annotation

Either random urine testing for albumin-to-creatinine ratio or timed urine testing can identify the presence of microalbuminuria. For random urine testing, the optimal collection time is the first urination of the morning. Strips are available to detect albuminuria as low as 20 mg/L but are not the recommended method, because they do not take into account possible errors resulting from alterations in urine concentration. Listed below are cutpoints for the various specimen types adopted from the American Diabetes Association.

Diagnosis of Proteinuria in Diabetes Mellitus

Condition	24-Hour Urine Collection	Alb/Cr	Timed Urine Collection
Normal albuminuria	≤30 mg/24h	<30 mg/g creatinine	≤20 micrograms/min
Microalbuminuria	30-300 mg/24h	30-300 mg/g creatinine	20-200 micrograms/min
Macroalbuminuria	≥300 mg/24h	≥300 mg/g creatinine	≥200 micrograms/min

Evidence

Strength of Recommendation: III, Level of Evidence: B (Kouri, 1991).

J. Is Urine Alb/Cr ≥30 mg/g Confirmed?

Objective

To establish a diagnosis of early diabetic nephropathy and to ensure that albuminuria is persistent, not transient, before committing the patient to treatment

Annotation

This cutpoint represents microalbuminuria. If the first specimen is ≥30 mg/g, repeat the test and be sure to have addressed the factors that may have transiently elevated the urine's albumin (see Annotation G). If the second specimen is also ≥30 mg/g, the patient has persistent microalbuminuria. If the second test is <30 mg/g, repeat the test a third time. "Multiple urinary measurements are necessary because as much as a 30 to 50 percent variability in day-to-day urine microalbumin measurements may occur."

Evidence

Strength of Recommendation: I, Level of Evidence: C (Murray, 1996).

K. Check 24-Hour Urine for Creatinine and Protein or Random Urine for Protein/Cr Ratio or Alb/Cr Ratio

Objective

To obtain the amount of proteinuria and to estimate the creatinine clearance rate

Annotation

The creatinine clearance rate approximates the GFR, but because of variability in collection, it is no more accurate than the commonly used Cockroft-Gault formula to assess the efficacy of the treatment:

(140 - age) x wt (kg) /72 x Scr (mg/dL)

Evidence

Strength of Recommendation: II, Level of Evidence: A (Toto et al., 1997), B (Cockroft et al., 1976; Rodby et al., 1995; Ginsberg et al., 1983).

L. Is Urine Protein/Creatinine ratio $\geq$300 mg/gm (0.3 gm/gm) or 24-Hour Urine protein $\geq$300 mg/d?

Objective

To help distinguish diabetic from nondiabetic kidney disease

Annotation

If the 24-hour urine protein excretion is <300 mg or the protein/creatinine ratio is <0.3g/g, diabetes is not likely to be the sole responsible cause of the elevation.

Macroalbuminuria is invariably the stage prior to loss of renal function and elevation of serum creatinine. In the absence of macroalbuminuria, other causes of renal failure should be investigated.

Evidence

Strength of Recommendation: N/A, Level of Evidence: B (Nelson, 1995).

M. Is Retinopathy Present?

Objective

To collect additional evidence confirming the diagnosis of diabetic nephropathy

Annotation

If the primary care provider finds retinopathy on an undilated eye exam, retinopathy is established. Findings such as microaneurysm, flame hemorrhage, soft or hard exudates, all indicate the presence of retinopathy.

However, if none is seen on undilated exam, a dilated exam is necessary to confirm the presence of retinopathy.

N. Refer to Nephrology

Objective

To obtain consultation from a nephrologist regarding the need for further workup, potentially including renal biopsy

Annotation

See Annotation E

O. Re-Evaluate for Nondiabetic Causes of Elevated Creatinine

Objective

To assure that other potential causes of renal failure are investigated

Annotation

The workup usually will include renal ultrasound to:

- Rule out urinary tract outflow obstruction
- Size the kidneys (small represents long-standing hypertension or intrinsic renal disease)
- Rule out anatomic anomalies (congenital, cysts, mass).

A postvoid residual urine can be helpful in identifying urethral obstruction (prostate, strictures) or cystopathy as a cause of lower obstruction. If hematuria is also present, visualization of the bladder may be warranted. The nephrologist can advise regarding the need for renal biopsy to rule out glomerulonephritis, collagen vascular disease, or other etiologies.

P. Counsel Patient on Reduced Protein Diet

Objective

To advise the patient that lowering his or her protein intake may have a positive effect on the progression of his or her renal disease

Annotation

"In people with type 1 DM and overt diabetic nephropathy, restriction of dietary protein has been shown to retard the progression toward renal failure. There is some evidence that this may also be true in type 2 DM. Therefore, a protein intake of approximately the adult recommended dietary allowance-0.8 g^{-1} kg body wt^{-1} day^{-1} (~10 percent of calories)-is recommended for individuals with evidence of macroalbuminuria."

A number of small studies have demonstrated a slowing of the rate of progression of type 1 diabetic nephropathy with a low-protein diet (0.6 to 0.7 g/kg/day). However most of these studies were relatively small, 11 to 35 patients. The largest study of the effect of low-protein diet on all renal disease, the Modification of Diet in Renal Disease study, did not show this effect to be significant. Only around 50 patients with diabetes were enrolled and insulin-using patients were specifically excluded. None of the studies cited above have been long enough to look at the effect of a low protein diet on progression to ESRD.

Although the value of a low-protein diet has not been adequately established, this Panel recommends offering it as an option in the treatment of diabetic nephropathy.

See Table R3 of the original document for a list of clinical trials evaluating the effect of dietary protein reduction on the course of diabetic nephropathy in type 1 DM patients with clinical proteinuria

Evidence

Strength of Recommendation: II-IIa, Level of Evidence: A (Ciavarella et al., 1987), B (Evanoff et al., 1989; Walker et al., 1989; Zeller et al., 1991), C (ADA, 1997).

Q. Does Patient Have <1 g/$_{g\ Cr}$ with BP $>140/85$ or >1 g/$_{g\ Cr}$ with BP $\geq 125/75$?

Objective

To identify hypertensive patients who may benefit from hypertension control management

Annotation

Aggressive treatment of hypertension has been shown to slow the progression of renal disease.

Evidence

Strength of Recommendation: II, Level of Evidence: B (Merlo et al., 1996), C (Roca-Cusachs, 1993; Hasslacher, 1997).

R. Are ACE Inhibitors Contraindicated?

Objective

To screen the patient for contraindications to ACE inhibitor use

Annotation

Absolute contraindications are:

- Pregnancy
- Hyperkalemia (advanced renal insufficiency or hyporeninemic hypoaldosteronism)
- Known allergy to ACE inhibitors

Relative contraindications are:

- Known bilateral renal artery stenosis
- Advanced renal disease

S. Start/Adjust Treatment with ACE Inhibitor. Check Serum Potassium Prior to Starting ACE Inhibitor and Repeat in 2 to 4 Weeks

Objective

To ensure that ACE inhibitors do not induce or aggravate hyperkalemia

Annotation

The use of ACE inhibitors in normotensive diabetic patients with micro- or macroalbuminuria has been shown to reduce albuminuria and slow progression of renal disease.

- Evidence for ACE inhibitors being effective in type 2 DM

  At least one long-term (7 years) randomized, placebo controlled trial and numerous other shorter term (6 months to 4 years) trials in normotensive type 2 DM patients have found a decrease in proteinuria with ACE inhibitor treatment. Evidence for efficacy of ACE inhibitors in type 1 DM seems to be conclusive.

- Frequency of monitoring post therapy

  "After initiation of therapy with an ACE inhibitor, the efficacy of this intervention should be monitored by assessing the albumin/creatinine ratio every 3 to 6 months. Because the urine albumin-excretion rate would be expected to increase by approximately 10 percent to 30 percent per year, stabilization of the albumin/creatinine ratio or a reduction in this ratio by up to 50 percent should be expected." It is also recommended to "check serum potassium and creatinine one week after initiation of therapy."

Evidence

Strength of Recommendation: I-IIa, Level of Evidence: A (Marre et al., 1988; Romero et al., 1993; O'Donnell et al., 1993; Bennett, 1995), B (Ravid et al., 1993).

T. Stop ACE Inhibitor Treatment

Objective

To ascertain whether side effects have occurred that warrant discontinuation of the ACE inhibitor

Annotation

Many patients present with a dry, nonproductive cough from ACE inhibitor use that resolves when this medication is discontinued. To avoid this side effect, one of the newer angiotensin II receptor agonists, e.g., losarten, may be used. Their specific efficacy in diabetic renal disease (as opposed to hypertension) is currently being studied. Recurrent hyperkalemia or a rapid rise in serum creatinine, even on small doses of an ACE inhibitor, is a second side effect concern. Allergic reactions such as skin rash may also warrant discontinuation.

U. Monitor 24-hour Urine or Spot Urine for Alb/Cr Ratio in 6 Months. Adjust Treatment and Follow-Up as Indicated

Objective

To decide whether renal disease is progressing on the current dose of ACE inhibitor

Annotation

If albuminuria is progressing or the GFR (as represented by creatinine clearance) is continuing to decline, a more aggressive treatment should be considered. The ACE inhibitor could be increased to the maximum recommended dose. If BP is rising, an additional agent could be added. Low-protein diet and glycemic control need to be reinforced.

V. Monitor for Serum Creatinine and 24-Hour Urine Protein and Creatinine or Spot Urine for Alb/Cr Ratio in One Year

Objective

To decide whether renal disease is progressing on the current regimen that includes ACE inhibitor, blood pressure control, glycemic control, and a reduced protein diet

Annotation

If renal disease is progressing, as evidenced by an increasing serum creatinine level, a decreasing creatinine clearance rate, or an increase in proteinuria, the treatment regimen needs to be reevaluated, including BP and glycemic goals.

Evidence

Strength of Recommendation: I-IIa, Level of Evidence: B (Mogensen, 1987; Ravid et al., 1993), C (ADA, 1994, 1995, 1997; Bennett, 1995; Gall et al., 1991; Murray, 1996; Ordonez & Hiatt, 1989).

Algorithm - Self-management and Education

Module M - Self-Management and Education

A. Patient with Newly Diagnosed Diabetes Mellitus?

Objective

To ensure that patients with newly diagnosed diabetes mellitus (DM) are provided with core competency education. For an overview of core competency (survival skills) information. See appendix M1, Core Competencies (Survival Skills)

B. Provide Information and Education on Basic Concepts, Core Competencies. Document Findings

Objective

To ensure that core competencies (survival skills) and other basic information are understood by patients with diabetes and enable them to safely self-manage their diabetes

Annotation

Primary care staff has limited time to provide in-depth education; however, it is critical to provide:

- Provide basic concepts and information based on core competencies for newly diagnosed patients
- Identify knowledge/skills deficit expressed in previous algorithms

Core competency education (survival skills) is directed at providing immediate education that will help ensure the safety of the patient until in-depth self-management education can be obtained.

The core competencies include:

- Acute complications (hyperglycemia and hypoglycemia)
- Medication education
- Basic diet principles
- Sick day management
- When to seek further assistance

Appendix M1 of the original document, Core Competencies (Survival Skills) for patient's with Diabetes, details the core competency content.

The core competencies are not substitutes for an in-depth self-management education program. Appendices M3, Suggested points of Contact for Patient Education/Nutrition/Self-management Programs; M4, Primary Care Staff Office Diabetes Education Resources and Tools; M7, List of Patient References: Diabetes Resources, lists resources for diabetes education. Patient education materials from these resources, as well as other patient education materials, can be made available to the patient in the office setting to assist the provider in addressing additional concepts and information not included in core competencies.

Results from the assessment of the patient's learning needs, abilities, preferences, and readiness to learn, should be documented. Cultural and religious practices should be included as well as emotional barriers, desire and motivation to learn, physical and cognitive limitations, language barriers, and the financial implications of care choices. The patient's understanding of the newly acquired education should also be assessed.

C. Refer for Comprehensive Self-management and Diet Education

Objective

To provide or refer for comprehensive self-management (SME) and diet education

Annotation

Diabetes self-management has been deemed necessary by most healthcare organizations to assist persons with diabetes a) in their day to day self-management demands; and b) with making informed self-care choices. This includes the provision of behavioral strategies that establish and maintain a healthy lifestyle. Since the diabetes clinical state fluctuates within individuals over their life span, education programs need to be comprehensive enough to provide clinically relevant knowledge and skills to facilitate implementation of the changing treatment plans.

Self-management education (SME), including medical nutrition therapy, is an interactive, collaborative, ongoing process involving people with diabetes and educators. As opposed to didactic education, SME is skill based learning. The four-step process comprises:

- Assessment of the individual's educational needs
- Development of an educational plan to meet the individual's identified needs
- Educational intervention directed toward helping the person achieve identified self-management goals
- Evaluation of the individual's level of attainment of the identified self-management goals

Leading experts in diabetes care and education revised the original National Diabetes Advisory Board (NDAB) Standards. The revised standards identify the following as essential curricula components for SME:

- Diabetes overview
- Stress and psychological adjustment
- Family involvement and social support
- Nutrition
- Exercise and activity
- Medication
- Monitoring and use of results
- Relationships among nutrition, exercise, medication, and blood glucose level
- Prevention, detection, and treatment of acute complications
- Prevention, detection, and treatment of chronic complications
- Foot, skin, and dental care
- Behavioral strategies, goal setting, and problem solving
- Benefits, risks, and management options for improving glucose control
- Preconception, pregnancy, and gestational diabetes
- Use of health care systems and community resources

Referral for in-depth SME and diet consultation (if separate from the diabetes self-management program) is recommended for all patients newly diagnosed with diabetes. Selection of the educational components must be tailored to patient needs.

The following three ways provide comprehensive education on self-management and diet:

- Refer for in-house comprehensive diet consultation-Medical Nutrition Therapy (MNT)-and self-management education program
- Refer to a comprehensive SME program in the community. An ADA recognized program is recommended, if available (see Appendix M3, Suggested Points of Contact for Patient Education/Nutrition/Self-management Programs)
- Conduct education in your clinical setting in the absence of an available comprehensive self-management program. Topics should be covered by the most qualified healthcare professionals with special knowledge in the topic area. A team approach is highly desirable and could include, but is not limited to, referrals to a dietician, certified diabetes educator, registered nurse, pharmacist, exercise physiologist, physical therapist, social worker, endocrinologist, or other specialized physician based on the individual patients' needs.

Evidence

Strength of Recommendation: IIa, Level of Evidence: B (Davidson, 1979; Franz, 1995; Jacobson, 1983; Miller, 1972; Rubin, 1998).

D. Determine Patient's Extent of Knowledge and Self-management Skill Deficit Based on Treatment Goals

Objective

To determine the education and skills enhancement needed to enable the patient to self-manage

Annotation

Assess the patient's knowledge of the diabetes disease process, treatment goals, management skills, cultural influences, health beliefs/behavior, attitudes, socioeconomic factors and barriers as each relates to the patient's ability to self-management and to determine the extent of his or her education and skills deficit. Choose the questions that relate to the clinical treatment goals/issues identified pertinent to the individual patient grouped according to treatment goals:

- Nutrition and meal planning
- Goal setting
- Home monitoring
- Foot care
- Exercise
- Medication
- Acute complications
- Psychosocial
- Preventive screening
- Treatment adherence
- Lifestyle

A panel of certified diabetes educators has compiled a list of initial questions to assist the provider (see Appendix M5, Questionnaire on Patient's Knowledge and Compliance). These questions are not to be interpreted as a validated instrument and may need to be adjusted to fit the patient's level of education and/or ability to comprehend what he or she is being asked.

Appendix M6, Patient Self-management and Knowledge Needs Assessment, includes the desired patient response to the questions in appendix M5, and suggested actions to take when the patient is unable to demonstrate knowledge/skills.

E. Does Patient Need Referral for Further Education or Intervention?

Objective

To identify patients who are at high risk for diabetes complications or need further educational intervention

Annotation

Because primary care appointments are frequently too short to provide adequate time to address background and educational issues, a referral or separate visit(s) to address the patient's needs may be required. This may involve sending the patient to the comprehensive self-management program, possibly for a second time. However it may be necessary to send the patient to another clinician/specialist for individual visit(s) to evaluate and address, an often complex combination of educational issues, treatment issues, coordination of care issues, psychosocial issues or financial issues. High risk

patients may benefit from these types of referrals. Decisions for referral are based on level of risk and extent of educational deficits.

Examples of conditions that may warrant risk-focused intervention are:

- Elevated HbA_1c (3 percent above the upper limit of normal or > 9.5 percent)
- Uncontrolled hypertension
- Serum creatinine level >2 mg/dL
- High risk feet
- Pregnancy; or planned pregnancy; or woman of child bearing age
- Poor eyesight
- Severe psycho-social or economic barriers
- Advanced age
- Intensive insulin therapy
- Recurrent hypoglycemia or hypoglycemia unawareness
- Recent hospitalization for diabetic ketoacidosis (DKA) or severe hyperglycemia

The need for risk-focused interventions may also have been identified through algorithms G, F, L, H, and E.

Deficiencies in any of the critical areas from the history section of Algorithm D Core may indicate patient knowledge needs in multiple areas and should trigger referral for comprehensive diabetes SME.

F. Refer for Risk-Focused Intervention or to Case Manager or to Appropriate Specialist

Objective

To determine which referrals are appropriate based on patient's needs and availability of providers, programs, and benefit coverage

Annotation

After explaining the basic concepts, if the primary care team determines that the patient does not yet understand concepts or would benefit from a more in-depth, risk-focused education or intervention, a consultation should be requested.

In some cases, more than an educational intervention is required. Patients at high risk may have needs beyond educational deficits and referral for focused attention from other services is indicated. Possible referrals could include, but are not limited to:

- Dietitian
- Certified diabetes educator or comprehensive Diabetes Self-management Education Program
- Case Manager
- Registered nurse

- Pharmacist
- Psychologist
- Exercise physiologist
- Physical therapist
- Social worker
- Endocrinologist

or other specialist based on the individual patient's needs, e.g., family counseling or social work. Case managers are a valuable resource for providing ongoing, detailed coordination of care for high-risk patients.

Evidence

Strength of Recommendation: IIa-IIb, Level of Evidence: B (Aubert et al., 1998; Sikka et al., 1999), C (Franz, 1995).

G. Reassess and Follow-Up as Indicated

Objective

Identify the frequency of patient appointments needed to evaluate educational effectiveness or reinforce education/self-management skills.

Annotation

When knowledge deficits still exist or a large number of lifestyle changes are necessary, frequent follow-up may be indicated. Panel experts recommend that recently learned diabetes skills or information be re-evaluated no longer than 3 months after initial instruction.

Single behavioral goals should be identified and prioritized to increase the likelihood of the patient adopting lifestyle changes necessary to achieve treatment goals.

H. Does the Patient Want More Information?

Objective

To address patient's desire (motivation) for additional information

Annotation

Patients often hear of developments, or may have specific questions, about newer treatment modalities. They may also decide they want to improve their glycemic control or their life style.

I. Provide Materials or Patient Reference List or Refer as Needed

Objective

To provide additional information in response to patients' questions about new treatments or advanced self-management skills that have been communicated from other persons with diabetes or the media

Annotation

When patients request additional information and it may not be essential for the caregiver to intervene professionally or refer to a specialist, Appendix M7 of the original document, List of Patient References: Diabetes Resources, provides the patient with adequate references.

Strength of Recommendation:

Level I: Usually indicated, always acceptable, and useful and effective.

Level IIa: Acceptable, of uncertain efficacy, and may be controversial. Weight of evidence in favor of usefulness/efficacy.

Level IIb: Acceptable, of uncertain efficacy, and may be controversial. May be helpful, not likely to be harmful.

Level III: Not acceptable, of uncertain efficacy and may be harmful. Does not appear in guidelines.

Grades of Evidence: Primary (Secondary)

A. Randomized (Other clinical studies)
B. Well designed clinical studies (Clinical studies related to topic but not in a population with diabetes)
C. Panel consensus (Clinical studies unrelated to topic)

Abbreviations

ACE - angiotensin converting enzyme

ADA - American Diabetes Association

AUDIT - Alcohol Use Disorders Identification Test

BCF - basic care formulary

BIDS - bedtime insulin daytime sulfonylurea

BMI - body mass index

BP - blood pressure

BPH - benign prostatic hyperplasia

CAGE - screening pneumonic for determining drunkenness

CVA - cerebral vascular accident

CHD - coronary heart disease

CHF - congestive heart failure

COPD - chronic obstructive pulmonary disease

CVD - cardiovascular disease

DCCT - diabetic control and complication trial

DM - diabetes mellitus

DQIP - Diabetes Quality Indicator Project

DTR - deep tendon reflex

ESRD - end stage renal disease

ETOH - ethanol

FBS - fasting blood glucose

FPG - fasting plasma glucose

g - gram

GDM - gestational diabetes mellitus

GFR - glomerular filtration rate

GHb - glycosylated hemoglobin

GU - genitourinary

HbA_1c - hemoglobin marker (A_1c)

HCTZ - hydrochlorthiazide

HDL - high density lipoproteins

HMG CoA - Hydromethylglutaryl coenzyme A

HOT - Hypertension Optimal Treatment study

HPLC - high pressure (liquid chromatography)

HTN - hypertension

IFG - impaired fasting glucose

IGT - impaired glucose tolerance

IRMA - intraretinal microvascular anomalies

JNC VI - Sixth Report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure

LDL - low density lipoproteins

LDL-C - cholesterol low density lipoproteins

LE - lower extremity

LE - level of evidence

MAST - Michigan Alcohol Screening Test

MI - myocardial infarction

MNT - medical nutrition therapy

NCEP - National Cholesterol Education Program

NGSP - National Glycohemoglobin Standardization Program

NIDDM - non-insulin dependent diabetes mellitus

NVD - neurovascular disc disease

NVE - neurovascular disease elsewhere or new vessels elsewhere

OGTT - oral glucose tolerance test

mg/dL - milligrams per deciliter

mmols/dL - millimoles per deciliter

MNP - medical nutritional therapy

PDR - proliferative diabetic retinopathy

PTH - parathyroid hormone

RD - registered dietitian

SLE - Systemic Lupus Erythematosis

SMBG - self-monitoring blood glucose

SR - strength of recommendation

TC - total cholesterol

TDD - total daily dose

TG - triglycerides

TIA - transient ischemic attack

TSH - thyroid stimulating hormone

UKPDS - United Kingdom Prospective Diabetes Study

UTI - urinary tract infection

VHA Veterans Health Administration

WESDR - Wisconsin Epidemiological Study of Diabetic Retinopathy

CLINICAL ALGORITHM(S)

Algorithms are provided for:

1. Core Algorithm
2. Algorithm - Glycemic Control
3. Algorithm - Hypertension Management
4. Algorithm - Eye Care
5. Algorithm - Foot Care
6. Algorithm - Lipid Control
7. Algorithm - Renal Care
8. Algorithm - Self-management and education

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The annotations which accompany the algorithms in the guideline document indicate whether each recommendation is based on scientific data or expert opinion. Where existing literature is ambiguous or conflicting, or where scientific data are lacking on an issue, recommendations are based on the expert panel's opinion and clinical experience.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Despite the high prevalence and even higher direct and indirect economic costs of diabetes, there is now incontrovertible scientific evidence that effective antihyperglycemic, antihypertensive, and hypolipidemic treatment produces substantial outcomes benefit.
- In addition, preventive care for diabetes can delay, if not prevent, a significant percentage of the instances of vision loss, chronic renal failure, foot ulcers and lower extremity amputations, as well as admissions for metabolic control.

Subgroups Most Likely to Benefit:

Glycemic Control

- In general, patients with very mild or no microvascular complications of diabetes and those free of major concurrent illnesses adversely affecting quality of life and survival are most apt to benefit from intensive treatment intended to achieve near-normoglycemia.

Hypertension

- Loop diuretics may be most effective in patients with creatinine clearance (CrCl) $\leq$40 to 50 mL/min (or serum creatinine $\geq$2.5 mg/dL)
- For patients who have already had a cardiovascular disease event and as secondary prevention, there is established benefit in lowering the low-density lipoprotein-cholesterol level to about 130 mg/dL.

POTENTIAL HARMS

General Side Effects of Pharmacotherapy

- Side effects of pharmacological therapy can include drug-drug interactions, hypoglycemia, and specific adverse drug effects. Patients may experience side effects from medications if adjustments are not made when patients undergo medical or surgical procedures, have a change in their condition, or develop an intercurrent illness.
- Patients may develop contraindications to continued use of a previously successful maintenance medication. Examples would include newly recognized renal insufficiency or severe congestive heart failure in a patient treated with metformin.

Specific Side Effects of Pharmacotherapy

- Sulfonylureas: Certain medications may interact with or potentiate the action of sulfonylureas (see Table G4c of the original guideline document).
- Biguanides (Currently available: Metformin): Patients at risk for lactic acidosis should not receive metformin. Metformin use should be avoided in patients with hepatic disease or excessive ethanol intake or in any patient with a

condition associated with hypoxemia, dehydration, or sepsis. Metformin use should be temporarily discontinued at the time of or prior to intravascular radiocontrast studies or surgical procedures. Monitoring renal function to prevent lactic acidosis, especially in the elderly is important. Use of metformin is associated with transient, dose-related gastrointestinal side effects such as diarrhea, nausea, vomiting, bloating, flatulence, and anorexia.

- Insulin therapy: Adverse effects may include hypersensitivity reactions, weight gain, and hypoglycemia.
- Alpha-glucosidase inhibitors (Miglitol, Acarbose): The patient should be advised of the transient, dose-related gastrointestinal side effects (diarrhea, abdominal pain, and flatulence). Initiating therapy at a reduced dosage may reduce these side effects. Reduction in plasma triglycerides may occur with miglitol use.
- Thiazolidinediones (â œglitazonesâ): Plasma volume has been shown to increase with these agents, causing reduction in hematologic parameters such as hemoglobin and hematocrit. Rosiglitazone and pioglitazone may induce ovulation in premenopausal anovulatory patients Increases in low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), and total cholesterol have been observed these agents. Weight gains of 1-4 kg may occur with these agents.
- Repaglinide: The most commonly reported adverse effect of repaglinide was hypoglycemia and was generally comparable to that seen with sulfonylureas.

Hypertension

Thiazides

- Hypokalemia may potentiate digitalis toxicity

Beta-Blockers

- Bradycardia, congestive heart failure, fatigue, insomnia, cold extremities, impotence
- Beta-blockers may mask symptoms of hypoglycemia
- Labetalol and carvedilol may cause postural hypotension; therefore standing blood pressure (SBP) should be monitored

Calcium Channel Blockers: Non-dihydropyridines (verapamil, diltiazem, mibefradil)

- Verapamil: Monitor for bradycardia and heart block. Doses >240 mg/d of verapamil tend to increase side effects with minimal added benefit.
- Diltiazem: may decrease sinus rate and cause heart block

ACE Inhibitors

- Hyperkalemia

Alpha-Blockers

- Initial doses should be given at bedtime to reduce the risk of syncope

Angiotensin II Antagonists (losartan, valsartan, irbesartan)

- Hyperkalemia

Centrally Acting Beta-Agonists (clonidine, guanabenz, methyldopa)

- Monitor for sedation (usually transient) during initial therapy with methyldopa or whenever the dose is increased.

Other Centrally Acting Agents (reserpine)

- Monitor for sedation, depression, nightmares, tremors, nasal congestion

Direct Vasodilating Agents (minoxidil and hydralazine)

- Monitor for reflex tachycardia with worsening angina, and for edema
- With hydralazine monitor for headache, dose related systemic lupus erythematosus (SLE)
- With minoxidil monitor for hypertrichosis, pericardial effusions
- Minoxidil or hydralazine should be used with diuretic and beta-blockers to reduce reflex tachycardia and edema.

Eye Care

- Beta-blockers are used most frequently, but while generally safe, they can be associated with the same complications as systemic beta-blockers.

Lipid control

- Antilipidemic drugs can have side effects, principally on liver function
- The most frequent main side effect of concern is hepatic dysfunction. If there is no drug-related hepatic dysfunction during the first year of therapy, hepatic enzymes can be reassessed periodically—generally once or twice a year.
- Muscle injury due to drugs is rare and is usually detected by complaints of muscle pain or soreness with concomitant elevations in muscle enzymes, mainly creatinine kinase.

Renal disease

- ACE Inhibitors: Many patients present with a dry, nonproductive cough from ACE inhibitor use that resolves when this medication is discontinued.

Subgroups Most Likely to be Harmed:

Glycemic control

- Patients with advanced microvascular complications and/or major comorbid illness may be less likely to show survival benefit, may continue to show progression of microvascular disease, and frequently may be at increased risk for severe hypoglycemic morbidity when normoglycemic control is attempted.

Insulin Therapy in Type 1 Diabetes Mellitus

- Patients with type 1 diabetes mellitus generally are more sensitive to changes in insulin dosage and far more susceptible to episodes of hypoglycemia than individuals with type 2 diabetes mellitus. According to a resource intensive controlled randomized trial (DCCT), for patients with type 1 diabetes mellitus treated on intensive insulin regimens the risk of severe hypoglycemic reactions was increased by 300 percent.
- Elderly patients are at a higher risk for drug-associated hypoglycemia, due to altered metabolism and excretion rates, impaired symptom recognition, and potentially attenuated counter-regulatory responses.

Biguanides (Currently available: Metformin)

- Elderly patients (> 65 years old) generally should not be titrated to the maximum dose as renal function decreases with age thereby increasing the risk of lactic acidosis with metformin.

Hypertension

Thiazides

- Hypotension, especially in the elderly

Alpha-Blockers

- Use cautiously in the elderly due to first dose syncope or dizziness

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- It should be recognized that this series of algorithms, as is true for most, cannot be used as a linear guideline for the recognition and management of diabetes mellitus and is not intended to supersede the clinical judgment of the provider caring for an individual.
- There is no intent to prevent practitioners from using their best judgment in the care of an individual patient. Rather, the intent is to establish verifiable treatment objectives for veterans with diabetes that will lead to a reduction in limb loss, visual loss, chronic renal insufficiency, and cardiovascular disease.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Explicit indicators to measure implementation system wide are a part of VHA's performance measurement system and are described in the Technical Manual on the VA's Web site.

RELATED NQMC MEASURES

- Diabetes mellitus: percent of diabetes mellitus patients with retinal exam by an eye care specialist, within specified time periods.
- Diabetes mellitus: percent of diabetes mellitus patients having annual sensory foot exam.
- Diabetes mellitus: percent of patients with diabetes mellitus having glycosylated hemoglobin (HgbA1c) less than 9.0.
- Diabetes mellitus: percent of patients with diabetes mellitus with blood pressure less than 140/90.
- Diabetes mellitus: percent of patients with diabetes mellitus having glycosylated hemoglobin (HgbA1c) greater than 11.0 or not done.
- Diabetes mellitus: percent of patients with diabetes mellitus with blood pressure greater than or equal to 160/100 or no blood pressure recorded in past year.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Management of diabetes mellitus in the primary care setting. Washington (DC): Department of Veterans Affairs (U.S.); 1999 Dec. 147 p. [185 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 Dec

GUIDELINE DEVELOPER(S)

Department of Defense - Federal Government Agency [U.S.]
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Diabetes Mellitus in the Primary Care Setting Working Group

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Department of Veterans Affairs Web site.

Print copies: Department of Veterans Affairs, Veterans Health Administration, Office of Quality and Performance (10Q) 810 Vermont Ave. NW, Washington, DC 20420.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Pocket Card for ready reference and Summary Algorithms suitable for posting.
- A CD-ROM and videotapes, as well as printed information regarding self-glucose monitoring and foot care are available in several languages.

Print copies: Department of Veterans Affairs, Veterans Health Administration, Office of Quality and Performance (10Q) 810 Vermont Ave. NW, Washington, DC 20420.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on February 9, 2001. The information was verified by the guideline developer on November 2, 2001.

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